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CARDIAC SYNDROMES COMPLICATING DIABETES AND THEIR TREATMENT

BY

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While it is true that common diseases must often co-exist in the same patient, the frequent association of heart disease with diabetes is the expression of a causal relationship. In the present paper the evidence for this statement will be examined. Thereafter an analysis will be made of 49 patients with heart disease and diabetes, with a discussion of the nature of the anginal and other cardiac syndromes developing, and typical clinical examples will be mentioned. Lastly, schemes of treatment for the various combinations of these maladies will be outlined.

That diabetes conduces to early, serious, and often fatal cardiovascular disease has been suspected for more than fifty years (Vergely, 1881 ; Frerichs, 1883), but pathological and clinical data have become available chiefly during the past decade. Blotner (1930) in necropsies of 77 diabetics found conspicuous disease of the coronary arteries in 45 per cent ; cardiac infarction was the cause of death in 10 per cent, the ages ranging from 13 to 85 years; these figures contrasted with a 21 per cent incidence of coronary sclerosis in 450 non-diabetics between the ages of 40 and 80 years. Warren (1930) found coronary thrombosis and cardiac infarction in 12 per cent of necropsies among diabetics, and commented on the frequency with which diabetics with advanced coronary sclerosis escaped angina. Root and Graybiel (1931), in a study of 210 cases of diabetes with angina, stated their experience that at necropsy every patient with a five-year history of diabetes had some degree of coronary sclerosis: they drew their 210 anginal patients from a series of 7000 diabetics, an incidence far in excess of that in an ordinary hospital population. Moreover, they found that diabetes exerted a levelling influence upon the sex incidence of angina (122 males and 88 females). For every patient in whom angina preceded diabetes, there were 21 in whom diabetes had preceded angina.

A comparison of the atherosclerotic lesions found at necropsy among 349 diabetics and those found in 3400 non-diabetics has been made by Root, Bland, Gordon, and White (1939). Coronary occlusion was much more frequent among the diabetics (23 compared with 6 per cent, between the ages of 40 and 60). In the same age group, 17 per cent of diabetics had coronary narrowing without occlusion, as against 12 per cent in non-diabetics. Clinical studies leading to similar conclusions have been made by Friedman (1935), who demonstrated aortic sclerosis by clinical methods in 75 per cent of 120 diabetics over 39 years of age. The high incidence of hypertension in diabetes has been shown by Root and Sharkey (1936); high blood pressure was present in 54 per cent of their series of 175 diabetics. They noted that coronary changes were absent only when diabetes was of less than three years' standing, and that advanced coronary sclerosis was twice as frequent in diabetics as in non-diabetics. Bell and Clawson (1928) found hypertension in 42 per cent of diabetics over the age of 50. Parallel to these clinical findings were the observations of Lehnherr (1933) who compared the cholesterol and calcium contents of aortas from diabetics and non-diabetics, and found exaggerated lipoid changes and greater calcium and phosphorus deposits in the diabetic aortas.

These pathological and clinical facts relating to the heart and aorta are consistent with the well-established relationship between diabetes and arteriosclerosis. That diabetes conduces to early and progressive general arteriosclerosis is no longer open to question in the light of the studies of Heitz (1923), Joslin (1927), Shepardson (1930), Priscilla White (1932), Leary (1935), and Root and Sharkey (1936). Shepardson gave radiological evidence of a 36 per cent incidence of calcification in the arteries of the legs in diabetics up to the age of 40, the average being 23 years. White gave similar results among diabetic children up to 15 years of age (19 out of 106 cases). Although these results strongly suggested that the diabetic condition conduced to arteriosclerosis, it could still be argued that arteriosclerosis and diabetes took origin from some common antecedent constitutional abnormality.

The work of Root and Sharkey (1936) gave additional evidence of a causal relation between diabetes and arteriosclerosis. They compared the necropsy findings of 175 diabetics of all ages with

those of 170 non-diabetics all over 40 years of age. A striking excess of arteriosclerotic lesions was found in the former group, but there was still the possibility that the arterial lesions began before the diabetes. To elucidate this point they investigated the arterial condition at necropsy of 23 diabetics of less than one year's duration. This group showed rather less arterial change than a control group of 170 non-diabetics. A similar disparity was recorded in the condition of the coronary arteries in the two groups. Moreover, as Root nnd Graybiel (1931) have pointed out, diabetes most frequently develops at 51 years, while diabetic angina occurs most commonly in the decade in which ten-year cases of diabetes are most numerous. These considerations, coupled with the levelling influence of diabetes upon the sex distribution of angina, point unmistakably to diabetes with its associated metabolic change as contributing to bring about arteriosclerosis in general and decrease of the coronary artery in particular. As Levine (1929) has demonstrated, diabetes must be accorded a place only subsidiary to that of high blood pressure among the morbid states conducing to coronary thrombosis.

Clinical Observations in Present Series

The present observations nre based upon 49 consecutive patients in whom diabetes co-existed with cardiovascular disease. The diabetes was of every grade from symptomless mild diabetes, proved by sugar tolerance curves, to gravely toxic or comatose stages. Cardiovascular disease similarly ranged from symptomless hypertension to acute coronary occlusion with high grades of shock. Diabetes accompanied only by peripheral arterial disease was not included. The sex distribution was fairly even: 26 females to 23 males. The average age of the women was 61, that of the men 62 years. The cardiovascular disease was always founded on hypertensive or degenerative lesions or both ; no example of rheumatic, syphilitic, or thyrotoxic heart disease in association with diabetes was encountered. But although the ætiology of the cardiac complications was strictly limited, a wide range of disorders of function was observed, such as left ventricular failure with cardiac asthma, congestive failure with œdema, and various forms of angina.

A very frequent accompaniment of diabetes was hypertension; this was present in 41 cases and in 3 others there was evidence that it had previously existed, making 44 out of the total of 49 cases. In general the grade of hypertension was far from trivial; in 31 instances the systolic blood pressure was 180 or more, compared with 13 in which it was under 180 mm. As striking as the prevalence of hypertension was the reduction in blood pressure during treatment. This fact and the observation that the reduction of pressure during stabilization of the diabetes was not uncommon, even in patients previously confined to bed, suggested that hypertension in these cases was in part attributable to the immediate metabolic fault.

Relation of Cardiovascular Disease to Diabetes

The patients comprising the present series fell naturally into certain categories. Some were aware of the existence of heart disease and diabetes at the time they first came under observation; of these a few had been or were still on insulin treatment, while others had never received this. Frequently a patient known to be diabetic presented himself with the initial symptoms of cardiovascular disease; rarely the converse relationship held. A well-defined group were those who had regarded themselves as well but now manifested symptoms of diabetes or of heart disease and were subsequently shown to possess a cardiopathy or diabetes respectively.

Group I. Patients known to have diabetes and cardiovascular disease (18 *of present series*).

These are often diabetics of long standing and the disease may be of a grade to require insulin treatment. It is well known that too great a dosage of insulin may provoke an anginal attack and this may culminate in coronary thrombosis. Equally, congestive heart failure or left ventricular failure may develop by the same mechanism. On the other hand, the dosage may be too small (actually, or relatively as a result of intercurrent infection). Coronary thrombosis is specially apt to occur in the diabetic, but there is evidence that inappropriate dosage of insulin may conduce to this accident. Some patients may never have had insulin treatment, although obviously in need of it when they come under observation. This commonly arises through the diabetes being at first slight and easily controlled by diet alone; gradually the fault becomes more severe and perhaps the patient has ignored warning sysmptoms of this process; finally, a cardiac attack discloses the untrolled or untreated diabetes. Evidence that the onset of effort angina, coronary thrombosis, cardiac asthma, or chronic congestive failure is attributable to the diabetic fault will be adduced below.

Group II. Patients known to have diabetes, developing cardiovascular symptoms (12 *cases*).

Patients of this group may seek advice on account of slight disorders, such as undue fatigue, shortness of breath, bouts of dizziness, or attacks of faintness. In a few cases one of the major seizures mentioned in the preceding section may be the first indication that cardiovascular disease has been developing.

Group III. Patients known to have cardiovascular disease, developing symptoms due to diabetes (5 *cases*).

The fact that relatively so few patients belong to this category is consistent with the established fact that diabetes is important in the ætiology of heart disease. In view of this relationship it would be surprising if many patients experienced symptoms of cardiac lesions before those of diabetes.

Group IV. Patients previously believed well, in whom the occurrence of a cardiac or a diabetic syndrome brings to light the existence of diabetes or heart disease respectively (14 *cases*).

It is remarkable that in so many patients diabetes and its cardiac complication may reach a fairly advanced stage without either of them causing obtrusive symptoms, but it is in keeping with the observation of Warren (1930) and other workers that necropsy in the diabetic may disclose advanced coronary sclerosis although there had been no symptoms of angina. In general it is uncommon for a grave diabetic development to occur in heart disease, or for a serious cardiac attack to complicate diabetes unless the patient has had early symptoms of one or other or both maladies previously.

While it might be more logical to consider the various cardiac disorders that may be observed in these groups of patients, it will save repetition if cardiac syndromes are reviewed in turn, the various circumstances in which each may occur being shown by reference to illustrative cases. The following will be dealt with : effort angina, coronary thrombosis, cardiac asthma, and congestive heart failure.

Various Cardiac Syndromes

Effort angina and spasmodic angina. This may be the natural and not unexpected expression of coronary sclerosis, and may develop in the manner so often seen in patients who have no diabetes. Nevertheless, while it is obvious that the heart of the diabetic must be provided with more than sufficient sugar for its needs, the failure to utilize this source of energy may lead to anginal attacks that are abolished by the use of insulin. Hetenyi (1927) has reported examples. This process has been observed in the present study in a man aged 53 in whom bouts of pain and oppression in the chest became much less frequent and severe as the fasting blood sugar fell from 315 to 219 mg. per 100 c.c. on treatment by insulin, 10 units twice daily, and a diet of 1800 calories. (Case I.)*

The rapid fluctuations of blood sugar that may take place from various causes in the diabetic patient who is on insulin treatment entail sudden alterations in the nutrition of the heart. As effort angina may correspond to these phases of imbalance, this indicates that anginal pain in the diabetic (and perhaps also in the non-diabetic) is not only related to ischæmia but also to metabolic disorders in the heart muscle, a phenomenon discussed in a previous publication (Shirley Smith, 1933). Angina produced by an excessive lowering of blood sugar in a patient taking too large a dose of insulin has been called " insulin angina ". Fortunately no syndrome of this kind was evoked during treatment in any cases of the present series.

Coronary thrombosis and cardiac infarction. Coronary thrombosis occurs with greater frequency among diabetics than among non-diabetics of the same age group. Its incidence is greater among diabetics who need, but are not taking, insulin. Thus an elderly female with long-standing glycosuria and hypertension developed increasing fatigue as a result of undue activity. After transient anginal attacks on three successive nights she developed coronary thrombosis, with congestive heart failure. By the use of digitalis and insulin therapy and the restriction of her fluid intake to 2 pints in 24 hours, she recovered and remained in good health for over three years when heart failure recurred. (Case 2.)

Patients who are on insulin treatment for diabetes are by no means protected from coronary thrombosis, even though the correct dosage seems to have been found. In a woman who was admitted with a ten-year history of diabetes, lethargic, dehydrated, and stuporous, the immediate danger was averted, but in spite of apparently successful adjustment of insulin dosage, signs of collapse recurred. Death ensued 19 hours after the onset, and necropsy confirmed the diagnosis of coronary thrombosis. (Case 3.)

When patients are on treatment by diet and insulin the sudden reduction or withdrawal of insulin may mark the onset of coronary thrombosis. In one instance the development of the attack followed

* Full case histories were submitted, but unfortunately had to be left out owing to reduction in the paper allowance.—Editor.

the omission of a dose of insulin the previous evening. A blood sugar level of 600 mg. per 100 c.c. showed that there had been progressive loss of control of the diabetes through inadequate dosage of insulin. (Case 4.)

It is not unusual for coronary thrombosis to occur as the initial expression of heart disease in a patient known to be diabetic. In some instances it develops with increasing hyperglycæmia and acetonæmia: in others diabetic coma may be the immediate sequel of acute coronary occlusion; e.g. a woman diabetic, aged 55, had an attack of coronary thrombosis, and about 60 hours after the onset she had become unconscious and extremely restless, and the blood sugar was found to be 650 mg. per 100 c.c.; she died very soon after the institution of treatment. (Case 5.)

While it is common for heart disease to develop in the diabetic the reversal of the order is comparatively rare. Only 5 examples were observed in the present series of 49 patients. In one, a female of 63, there was a history of effort angina for three years; during an acute pulmonary infection glycosuria was observed for the first time. (Case 6.) In another, a physician aged 57, there was undue fatigue six months after recovery from coronary thrombosis; he was found to have a low renal threshold, but the fact that his condition conspicuously improved with reduction of carbohydrate intake suggested that a fault of metabolism also existed. (Case 7.)

Coronary thrombosis often occurs without any warning symptoms of heart disease, and routine examination at the time may bring to light the existence of diabetes. This sequence of events was recorded in a female, aged 54, who complained essentially of pain in the left arm. Routine examination disclosed diabetes; she was admitted to hospital with evidence of a recent TIII type of cardiac infarction. She recovered and was discharged on a weighed diet of 2000 calories and 10 units of insulin daily, which allowed intermittent glycosuria. Death occurred suddenly a few months later. (Case 8.)

The intensity of arterial disease and its rapid progress in the diabetic offer an obvious explanation of the frequency with which anginal syndromes are observed. When cardiac breakdown occurs in forms that represent myocardial as distinct from coronary failure, the relationship is not so clear. In some patients in the present series, cardiac asthma was a circulatory expression of uncontrolled diabetes, suggesting that left ventricular failure might result from an untreated or a badly corrected fault in carbohydrate metabolism. Syndromes of this order suggest that diabetes exerts a deleterious effect on the myocardium, not only by virtue of coronary sclerosis but also through direct impairment of the parenchyma of the heart. That general heart failure with congestion and œdema may be the consequence of untreated diabetes will be suggested later, but the fact may be referred to at this point as demonstrating further the myocardial (as distinct from coronary) damage that may develop.

Cardiac Asthma. Cardiac asthma, following the aggravation of a latent diabetes associated with long-standing hypertension, was observed in the following instance. A woman, aged 41, had severe hypertension, and was seen at intervals for five years, glycosuria being found on one occasion. Twenty-four hours after a motor accident in which she was shocked but not injured, she experienced thirst and on the following night had cardiac asthma. Investigation disclosed severe diabetes. At the time of discharge on a fixed diet of 2000 calories, with insulin, 7 units twice daily, she was free from cardiac or diabetic symptoms, but showed intermittent glycosuria. (Case 9.)

It is not surprising that left ventricular failure and ultimately general congestive failure sometimes succeed effort angina in diabetes, as this sequence of events is commonly seen in coronary sclerosis without diabetes. In Case 10 cardiac asthma was the presenting symptom at the time of admission. A male, aged 58, had been a diabetic taking insulin for 7 years. For 18 months he had experienced effort angina. Cardiac asthma had supervened, and later signs of congestive heart failure. After admission to hospital and adjustment of insulin dosage, the paroxysms of dyspnœa came to an end and the signs of failure vanished. These events might be explicable on the basis of rest alone, were it not for the fact that rest had been employed without success prior to admission and that in hospital no relief from the cardiac asthma was obtained until adjustment of insulin dosage had been effected.

In another instance a woman, aged 60, had suffered for several years with diabetes and hypertension. Paroxysmal dyspnœa, chiefly nocturnal, developed, and relief from these distressing attacks synchronized with adjustment of the insulin dosage and diet. (Case 11.)

Congestive heart failure. While coronary arterial disease finds its most characteristic expression in anginal attacks of various kinds, it may culminate in congestive heart failure without painful episodes at any time. The development of failure in the diabetic would therefore not be surprising, and it might be regarded as entirely independent of the diabetic state except in so far as the latter conduced to coronary sclerosis. The disturbances of cardiac nutrition in diabetes may play a part in the development of failure, and stabilization may bring improvement in the circulatory condition. A man of 69 was admitted with congestive heart failure; he had been diabetic for 33 years. Severe dyspnœa persisted in spite of control of the hyperglycæmia and acetonæmia. Blood sugar examination showed that too great a reduction had been secured (56 mg. per 100 c.c.). A reduction in insulin

dosage allowed the blood sugar to rise to 222 mg. and signs of failure progressively disappeared. Failure re-appeared a month or two later, and on several occasions during this phase intravenous injections of glucose relieved severe paroxysms of dyspnœa. (Case 12.)

In another case of congestive failure following cardiac infarction, a choice had to be made between a free fluid intake to combat impending coma, and a restricted intake indicated by the orthopnœa and congestive failure. Further reference to the therapeutic dilemma is made hereafter in the consideration of treatment.

Treatment of the Cardiac Diabetic

As has been shown, the syndromes resulting from the cardiac complications of diabetes are of great variety. They are in fact often the same as those met with in patients who are not diabetic; in these treatment will be primarily directed to the circulatory condition, but treatment of the metabolic fault may never be ignored with impunity. In others the clinical features represent a blend between the effects of the cardiovascular disease and nutritional and toxic consequences of the diabetes; here treatment will call for an appraisal of the relative importance of the two elements: since the requirements of the one may be at variance with those of the other, great difficulty may be experienced in deciding upon the most suitable scheme of treatment. In yet others circulatory collapse of the second type described by Frerichs (1883) may complicate diabetic coma without any indication of congestive failure or coronary thrombosis. Experience shows that many of such patients may in the initial grave cardiac attack succumb within a few hours or days, the falling blood pressure and progressive collapse resisting all therapeutic efforts. The treatment of syndromes of this type has been studied by many workers (Labbe & Boulin, 1928 & 1933; Lawrence, 1933; and Clerc, 1934). Equally, the patient may be treated with the necessary precautions to be mentioned below, may make great improvement in the heart and diabetes, and yet may die suddenly without obvious immediate cause when he appeared to be well on the way to convalescence. These difficulties have been described by several observers (Haynal, 1925; and Soskin, Katz, Strouse, & Rubinfeld, 1933).

When a cardiac disease such as effort angina supervenes in a diabetic whose condition has been long recognized and kept under control, treatment will naturally first be directed to the necessary adjustments in the mode of life and to appropriate medicinal measures for the relief and prevention of pain. Nevertheless the development of angina will prompt an immediate survey of the diabetic state. While it has long been regarded as unwise to treat vigorously by diet diabetes in later life, it is specially dangerous to treat diabetes in the cardiac patient as a pure problem of diabetic stabilization. Sudden alterations of blood sugar by diet or insulin are not well tolerated. Treatment on the metabolic side will therefore be directed essentially to the avoidance of acetonæmia; if glycosuria persists in spite of qualitative or maintenance dieting, insulin may be used, but always in less quantity than would be employed if the same patient were free from signs of a cardiac fault. In general, it is safer for these patients to live with a moderate hyperglycæmia and to have glycosuria from time to time, than to be strictly controlled and rendered constantly free from sugar. This is because the myocardium may depend for its nutrition upon hyperglycæmia off-setting the deficient coronary flow.

Diet will be an important element in the treatment of all cardiac diabetics. Sometimes general and qualitative restriction (of bread, sugar, potatoes) is all that is required, but in many cases a full quantitative system will be necessary, with the number of calories laid down. The construction of such a diet with sufficient variety will not be difficult on the Lawrence line-ration scheme. Cardiac diabetics and in fact all diabetics should restrict foods of high cholesterol value such as eggs, cream, butter, cheese, and brains.

More complex situations arise when the diabetic develops such a condition as congestive heart failure or left ventricular failure with cardiac asthma. Here again the cardiovascular syndrome may be no different from one that might be seen apart from diabetes, and may seem to bear little relation to the metabolic fault, but as we have endeavoured to show in the cases mentioned, the therapeutic test may indicate that a close relationship exists between the circulatory breakdown and some maladjustment or failure of management of the diabetes. If no insulin was previously needed it may become necessary, owing to the increased basal metabolism in heart failure, to fever which sometimes accompanies failure, or to the disorganization of digestion and assimilation caused by congestion. On the other hand, if insulin were being taken the dose might need to be increased or decreased. Aggravation may be due equally to excess or deficiency of insulin.

Estimations of blood sugar (both fasting and three-quarters of an hour after a meal) coupled with frequent examination of the urine for sugar and acetone bodies will be essential. The ferric chloride (Gerhardt) test will in the first instance give more assistance than the Rothera test by providing a demarcation between grosser and milder grades of ketosis. If the ferric chloride test and clinical features show that there is little or no ketosis, the immediate danger of the patient is little more

than might be attributed to the heart failure alone. A careful review of the metabolic condition and analyses of blood and urine will be essential, and it may or may not be found necessary to give insulin or to adjust a dosage previously in use. In any case rather less insulin will be given than would be the case if no cardiac lesion were manifest. If the ferric chloride test is positive, and particularly if other indications of severe ketosis are present (rising pulse, abdominal pain, furred tongue, and headache), treatment of the diabetes will become of preponderating importance and urgency. The intake of fluid by mouth will be increased to six or eight ounces each hour, and insulin and glucose in the proportion of one unit of insulin to rather more than one gram of glucose. As the occasion will be one of great urgency, no accurate weighing of glucose will be practicable; roughly, a full (not heaped) tablespoonful of glucose contains fifteen to sixteen grams. Therefore a dose of twenty-five or thirty units of insulin would be suitably combined with two tablespoonfuls of glucose; these doses might be repeated once or more at intervals of two to four hours according to the needs of the individual case. Insulin will usually be given intramuscularly, but may be given intravenously if the condition is grave; the glucose will be given orally whenever possible, but if not, by rectal or intravenous infusion. It is obvious that each case will require assessment on its merits and that no hard and fast rules can be laid down. Nevertheless, the following points are of great importance in all cases in which a cardiovascular lesion of more than trivial grade is accompanied by diabetes with ketosis or impending coma.

1. The situation is grave and therapy urgent.
2. No time should be lost awaiting the results of laboratory investigations.
3. Immediate attention should be paid to the essentials of treatment for the diabetic complication, by the provision of warmth and rest, the increase of fluids by mouth, and the provision of stimulants, such as hot coffee or tea.
4. The use of insulin, coupled with more than balancing amounts of glucose added to the drinks or the infusions, is important.
5. From the cardiac standpoint warmth and rest are equally essential, the degree of recumbency depending upon the patient's wish.
6. Repeated examinations of urine will be necessary; it should not become constantly sugar-free but the aim is to abolish ketosis; blood sugar (fasting) should be estimated every few days and levels lower than 130 or 140 are to be avoided.

The association of diabetic coma with coronary thrombosis is one of the most desperate medical emergencies. The combination may take the following forms: coronary thrombosis may occur in a previously stabilized diabetic and induce coma; a diabetic may become unstabilized through some lapse in treatment or diet, or through some intercurrent infection, and then develop coronary thrombosis. In other cases the patient passes insidiously into diabetic coma with associated symptoms suggesting coronary disorder (pain or oppression in the chest); in these it may only be the course of events that will show whether or not a coronary occlusion has occurred. If it has, there will be either a fatal issue or a very protracted and dangerous illness; if it has not, the treatment directed to the coma will usually be followed by very rapid recovery. Neither the electrocardiogram nor its evolution in serial records is of conclusive help in this diagnosis, because in coronary thrombosis no change may be seen in the first few days (which are important ones from the standpoint of treatment), while in severe diabetes without coronary complications cardiographic changes very similar to those of coronary occlusion are sometimes found (Shirley Smith & Hickling, 1933; and Bellet & Dyer, 1937); however, the evolution in serial records is rather different in this case.

The problem of fluid administration is often difficult and sometimes insoluble in the treatment of heart failure associated with diabetes, of coronary thrombosis complicated by diabetes, and of diabetic coma or impending coma when severe heart disease exists. It is accepted that in congestive heart failure the fluid intake should be limited to 25 or 30 oz., and the same rule applies to treatment in the early days of acute coronary occlusion which has produced more than trivial constitutional upset. At the same time in each of the three examples cited, the appropriate treatment of the diabetes demands administration of perhaps four or five pints of fluid in the twenty-four hours, or if dehydration has developed, double these quantities, even if part has to be given by rectal or intravenous routes. The impossibility of reconciling these diametrically opposed requirements in the same patient is the reason why treatment is so often unavailing and why combined maladies of these kinds are so lethal.

In spite of these obvious difficulties there are certain general principles underlying fluid administration which should be observed in constructing a scheme of treatment.

In congestive heart failure accompanied by severe diabetes it is better to risk the development or increase of œdema than to allow progressive hyperglycæmia and ketosis. It will therefore be better to give sufficient fluid (in addition to other medication such as insulin) to minimize the risk of coma. Consequent œdema may be later dispersed by the mercurial diuretics, whereas increasing ketosis will

certainly aggravate failure even though no œdema exists. If diabetic coma is present the intravenous route must be used for the administration of fluid and glucose. The signs of dehydration denote a total fluid lack of perhaps 10 to 12 pints, and large quantities of fluid must therefore be given in a relatively short time (Lawrence, 1930). In Case 4 of the present series there was no doubt that the intravenous infusion of 10 per cent glucose saline helped in the relief of dangerous collapse due to the combined effects of severe diabetic ketosis (blood sugar 600 mg. per 100 c.c.) and coronary thrombosis.

Summary

The evidence proving that diabetes conduces to early and severe arteriosclerosis and, specially, to coronary arterial disease and coronary thrombosis has been reviewed.

The clinical features of 49 consecutive cases of diabetes associated with heart disease have been analysed. The sexes were fairly evenly represented; the average age of the men was 62 years, and that of the women 61 years.

Hypertension was present in 44 of the 49 patients (almost 90 per cent); in 31 instances the blood pressure was 180 mm. or more. As is usual in hypertension uncomplicated by diabetes, the blood pressure frequently dropped swiftly and considerably on confining the patients to bed. Reasons have been given for believing that hypertension in the diabetic was in some degree directly attributable to the metabolic fault.

A study was made of the manner in which angina of effort, spasmodic angina, coronary thrombosis, left ventricular failure, and congestive heart failure supervened in diabetics. Some case histories illustrating these events and showing the relationship between the diabetic state and the cardiac development have been summarized.

As a rule, patients with diabetes and one or other form of angina or heart failure were found to derive benefit from any necessary readjustments of regime or insulin dosage. Controlled observations were not, for obvious reasons, generally possible, but in a few patients, in whom this adjustment *only* was made, deterioration in the heart condition was replaced by improvement.

It has been concluded that while the lives of patients with disease of a coronary artery are at serious risk those of the "cardiac diabetics" are even more precarious. Coronary thrombosis in the diabetic is extremely hazardous.

Methods of treating cardiac complications in diabetes have been reviewed. The requirements of diet, fluid, insulin, glucose, and remedies directed to the heart have been considered. The well-known principle, that in patients with heart disease sudden reductions of blood sugar by diet or insulin are not well tolerated, has been endorsed in the present study. In general the use of insulin will be in such dosage as may be necessary to abolish acetonæmia and reduce severe hyperglycæmia. To use insulin to procure stabilization or exact control of the diabetes in patients with additional heart disease is to court disaster.

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CONGENITAL HEART BLOCK WITH DEXTROCARDIA

BY

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From the Highlands and Islands Medical Service

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Stein and Uhr (1941), describing congenital heart block in a girl of 3, bring the total of reported cases to 55. Apparently the number that are recognized and reported is still not great, since Campbell and Suzman (1934) analysed 53 which they accepted as fulfilling the criteria of diagnosis. Associated anatomical defects of the heart always seem to be present, and, as might be expected, septal defects are common, if not invariable. It has not been suggested that any case of incomplete heart block is congenital: partial and transient heart block is, of course, common enough in the acute infections, but if it should become complete, the patient usually dies. Fishberg (1940) saw one patient who survived with complete block that was apparently due to diphtheria, and quotes Stechner's study of 19 others, all of whom died. White (1937) thinks acquired cases apart from coronary disease are rare. The age of the patient is therefore a fair indication of the ætiology of complete heart block that persists, i.e. coronary disease in middle age and congenital defect in childhood and early adult life, and this rule will be subject to few exceptions. Writers have rather tended to insist that the cause of complete heart block in children and young adults should be assumed to be infection unless there is proof of its congenital origin, and Yater (1939) gives several criteria for the diagnosis. It seems likely, however, that most, if not all, cases of complete heart block in children and young adults are congenital, and the mere history of a severe infectious disease is no proof of ætiology. There must be few children in whom a history of one or other of the infectious diseases cannot be discovered, and one would need to have seen the appearance of block during the course of the infection to assume that this had been responsible. Such an observation, of course, has often been made in diphtheria, but survival after its appearance must be rare. The existence of *any* other evidence of congenital heart disease would be strong presumptive evidence that the heart block was also congenital. For example, Bower (1939) reports two cases as discovered after severe measles, but both had systolic murmurs that were probably due to septal defect.

A case of congenital heart block, with dextrocardia as part of a complete transposition of viscera, is here reported; she had the further peculiarity that she came under my notice with an acute primary tuberculous infection, and later developed extensive pulmonary tuberculosis, which, however, shows a strong tendency to heal. The association of complete heart block with dextrocardia must be very rare; I have only found reference to one other case (Yater, 1929). My patient had also the signs of septal defect.

Brown (1939), making a rather narrower selection of cases of complete heart block than that of Campbell and Suzman (1934), accepts 44 as being congenital, of which 27 had clear signs of a septal defect, confirmed in 5 by autopsy. He considers the rarity of congenital complete heart block fully explained by the fact that the A-V bundle develops in the fœtus before the formation of the septum, so that a defective septum is unlikely to interfere with conduction. The heart rate is not so slow as it is in adult acquired block, and may increase to 80 under certain conditions. The ordinary ventricular rate at rest is usually about 50; it is more easily increased by stimuli than in acquired heart block, and this explains why, unless a special search is being made for such cases, the condition may easily be overlooked. The subjects of congenital heart block may pass through a medical examination without the block being discovered.

Case Notes. H. G., aged 20, was admitted to the Royal Northern Infirmary on July 11, 1939. Three weeks before, there had been an eruption on the legs described as "a few small hard red tender spots," and at the same time she had pain in the legs on movement; a week after this she had a succession of rigors and a pain in her chest with some shortness of breath. It had been known for some years that she had dextrocardia, and exertion had always made her breathless and cyanosed. There was no history of any relative having been affected in the same way. The parents were not related and had neither dextrocardia nor heart block. Information about other sibs was merely second-hand from the girl's mother, i.e. she had never heard of any congenital heart peculiarity.

When admitted she had slight fever (temperature 99·5 F.), but was in no discomfort. She was cyanosed, but respiration at rest was quite peaceful. There was obvious clubbing of fingers and toes. Complete transposition of viscera was present (Fig. 1). There was a dorsal scoliosis, the heart's apex

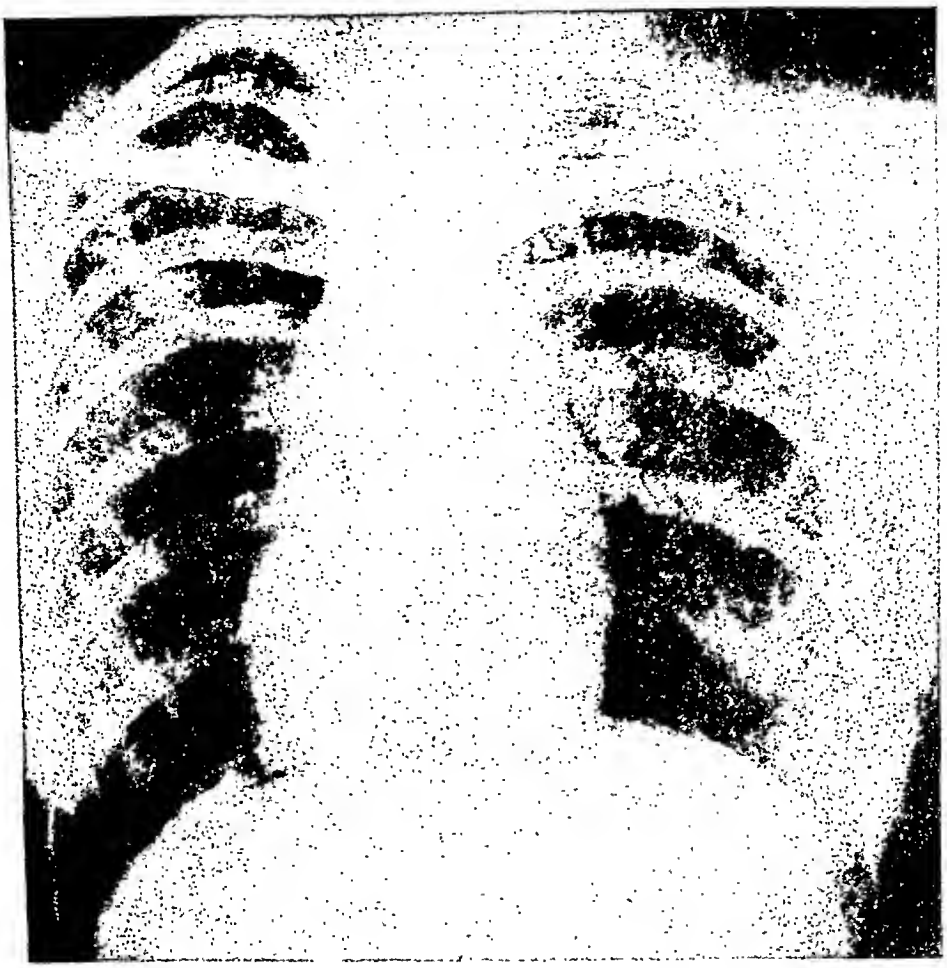

FIG. 1.—The chest in 1942, showing the development of tuberculous cavitation; there is also dextrocardia and enlargement of the "right" or pulmonary side of the heart, both of which had been present in the picture taken in 1939.

was to the right, and a loud rough systolic murmur was audible all over the præcordium with maximum intensity over the second right costal cartilage; there were no diastolic murmurs. The rhythm was regular, the rate 80, and the blood pressure 110/60 in the arms. The spleen and liver could not be felt, but there was dulness to percussion over the presumed site of the liver on the left side, and a small area of dulness over Gairdner's line (on the right side). No signs remained of the eruption on the legs and there were no petechial spots or hæmorrhages in the retina. A catheter specimen of urine showed a few red cells. The sedimentation rate (Westergren) was 80 and remained near this figure on repeated examination during her stay of four weeks in hospital; blood cultures were sterile. The cardiogram (Fig. 2) showed complete dissociation of auricle and ventricle, inversion of P I, and a deep Q I characteristic of the "mirror" picture of visceral transposition. T I, however, was positive. There was right axis deviation, which was consistent with hypertrophy of the pulmonary side of the heart due to septal defect.

The ventricular complex nowhere suggested an origin below the bifurcation of the bundle : this is to be expected, and is a usual feature of congenital heart block (Lampard, 1928). The auricular rate was 90–100 and the ventricular, 45–50.

The temperature fell to normal after 24 hours and the heart rate decreased until it reached its habitual frequency of 48 to 52. Exercise and subcutaneous adrenalin had no influence on the heart rate. The patient went home, and was kept in bed for two months: I saw her again three months after she left hospital, when she was getting about, in no distress.

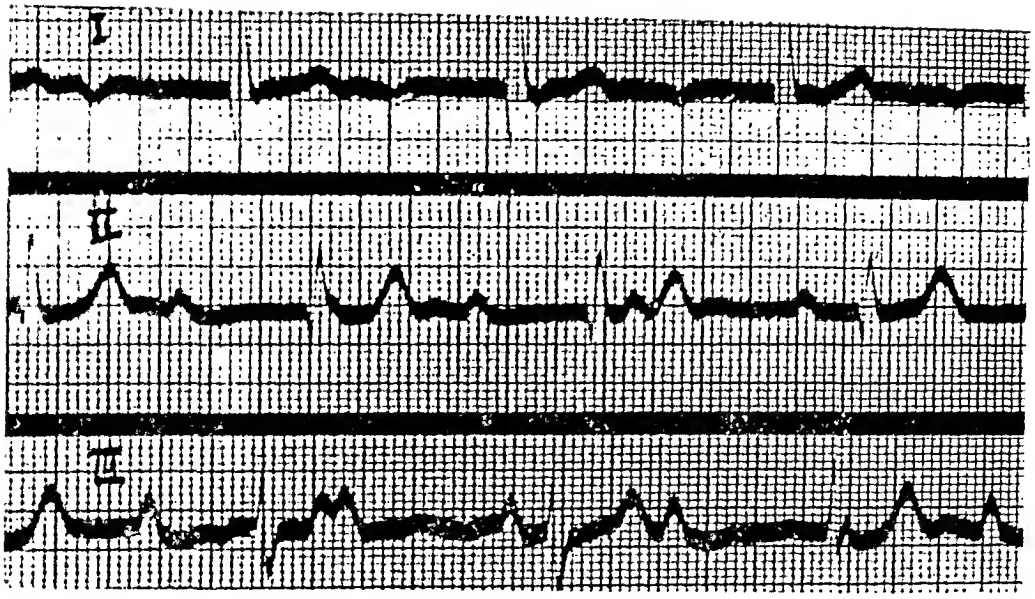

FIG. 2.—Standard leads showing dissociation of auricle and ventricle, inversion of P_1, and right axis deviation.

I did not see her again until May, 1941, when hæmoptysis occurred: she had been working regularly as an accountant's clerk for more than 18 months, and was in good health until she was moved to a northern town in mid-winter, where the heating arrangements were poor in her lodgings: she developed a cold and cough, which continued for some weeks, when the sputum became frothy and bright red. No evidence of heart failure was found, and there were no definite signs to be made out in the lungs. She was reluctant to go to hospital but reported after some weeks, when an X-ray showed scattered infiltration in both lungs, and the sputum contained tubercle bacilli. The sedimentation rate was now 60. She remained in hospital for two months during which time her sedimentation rate fell to 21, and she then returned home, at her own desire, practically symptomless. Reviewed in July, 1942, her health was as good, she thought, as it had been before her first hæmoptysis; an X-ray showed cavitation in both upper lobes, but with a hardening of all the pulmonary shadows; there was no sputum, and the sedimentation rate was 15.

Brown quotes Abbot (1927) for the maximum age attained in congenital heart block as 20 years. My patient is already 23 and, apart from her tuberculosis, is in good health. Except to anatomists and embryologists, the interest of the condition lies mainly in the effect on the subject's functional capacity. Most writers on the subject agree that the expectation of life is governed rather by the associated heart defects than by the block. While the relative inelasticity of the heart rate must obviously limit the subject's power of sustained muscular effort, the impossibility of damaging tachycardia may prevent some wear and tear.

SUMMARY

A patient with congenital heart block, dextrocardia, and probable septal defect is reported. She also developed extensive pulmonary tuberculosis, but showed a good tendency to recovery, and attained the age of 23 with good functional capacity equal to office work. Her ventricular rate was about 50, but rose to 80 during fever: it was not influenced by exercise or adrenalin.

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CONGENITAL HEART BLOCK WITH ATRIAL AND VENTRICULAR SEPTAL DEFECT

By A. A. FITZGERALD PEEL

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The combination of atrial septal defect with congenital complete heart block is of sufficient rarity to justify publication of the following case.

Case report.—A woman, aged 46, unmarried.

As far as can be ascertained, no abnormality was noted during the first five years of life. When the patient was 5, her mother died suddenly from heart disease, whereupon her grandfather had the patient medically examined ; her heart was said to be weak and she was put to bed for a month. Shortly after this she had scarlet fever and then diphtheria, and was very ill with the latter. At school she was short of breath and was unable to run ; she remembers that her face was highly coloured, and that she was repeatedly off school for a week at a time. After leaving school she did office work for seven years ; she occasionally had to take an afternoon's rest, but was seldom off for longer. For the next few years she was at home, and enjoyed fairly good health, but suffered from " slight attacks of breathlessness and dizziness " from time to time. In 1930 she underwent an operation for strangulated hernia.

In 1934 she was admitted to hospital. She had " felt seedy " on the previous day, and on going to bed became breathless and dizzy; nevertheless she was able to get up and go out shopping next morning; on her way home, she called on a doctor who sent her to hospital, where she remained for ten days. At that time she was described as well nourished, very highly coloured, and with slight cyanosis. The heart was enlarged. There was a loud blowing systolic murmur all over the præcordium and conducted to the axilla; the sounds were well heard in addition to the murmur, and the first sound was reduplicated at the apex. The pulse rate was usually 46, never less than 44, and only once as high as 50 during her stay in hospital. A cardiogram showed complete auriculo-ventricular block with an auricular rate of 60 and ventricular rate of 45·6; in lead I, the P waves were upright, but QRS and T were completely inverted; in leads II and III the complexes were normal. There was no polycythæmia, the red cell count being 4,760,000 and hæmoglobin 95 per cent. There is no record of the X-ray findings and the films are no longer available.

In 1936 she took work as a housekeeper, a job which she still retains. It was at this time, at the age of 40, that she began to feel more breathless and found she was becoming more blue. She noticed that her hands were blue, whereas hitherto the high colour was confined to the face. She could walk smartly for short distances without dyspnœa, but could not go far. At her work, she had to sit down and rest from time to time, but she had not had to go on the sick list. Within the last few months she has had a harsh cough from time to time, and has been hoarse for a day or two at a time; some two or three months ago she had a blood-stained spit, and recently the spit has on occasion been slightly streaked with blood. She has never fainted, and she has never had anything resembling a Stokes–Adams attack.

Examination. She is a small, underdeveloped, thin woman with a slight scoliosis. There is intense injection of the malar regions with small venules visible, the colour being a reddish violet; in addition to this, there is cyanosis of the lips and hands. The heart is considerably enlarged, the apex being in the mid-axillary line, six and a half inches from the mid-line. The first sound at the apex is loud and accompanied by a soft blowing murmur; the second sound is reduplicated. The murmur can be followed medially for a short distance, but not further than the mid-clavicular line; there are no murmurs elsewhere. The pulse was 48 and regular, save for an occasional extrasystole. Blood pressure was 124/80 in February and 114/74 in September, 1942. The lungs showed generalized bronchitis in February, but were clear in September. There was albuminuria, but neither enlargement of the liver nor œdema.

The electrocardiogram (Fig. 1), substantially unchanged since 1934, shows complete auriculo-ventricular block with an auricular rate of 68 and a ventricular rate of 46. The auricular complexes are upright in all leads; the ventricular complexes (QRS and T) are inverted in lead I, resembling those seen in dextrocardia.

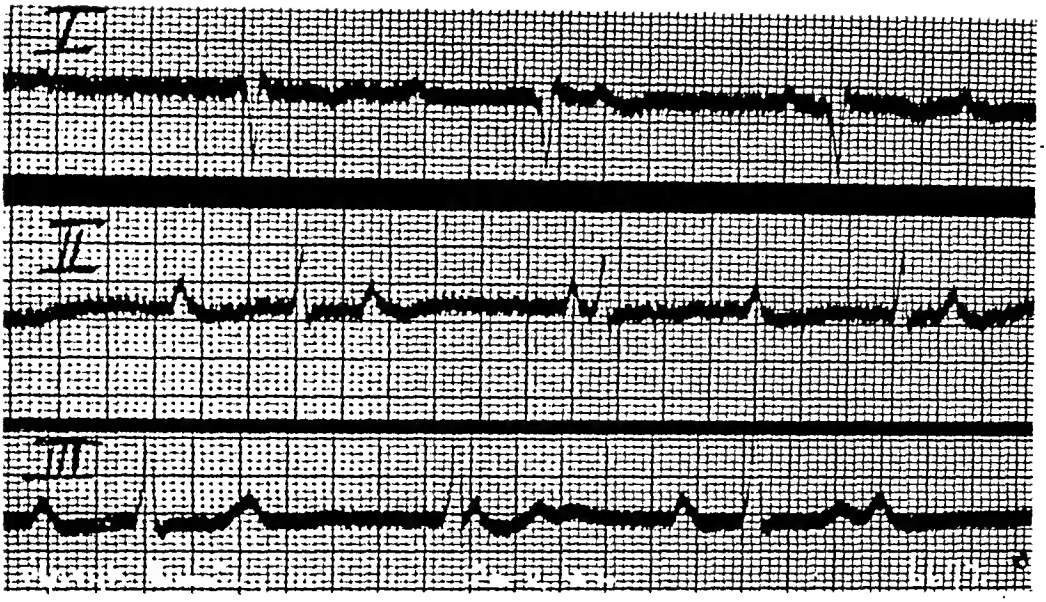

FIG. 1.—Electrocardiogram showing complete heart block and changes somewhat similar to those found with dextrocardia.

Skiagrams of the heart in the antero-posterior and oblique positions are shown in Fig. 2-4. The report on screening (Dr. J. G. McWhirter) is as follows :—" The transverse diameter of the cardiac shadow is increased beyond normal limits and the appearances suggest that this is due to right ventricular hypertrophy. The main branches of the pulmonary artery are enormously dilated and pulsation is easily seen in them. The main pulmonary artery is large and is easily seen in the right oblique position causing some indentation of the œsophagus. The lower end of the œsophagus is also displaced backwards and to the right by an enlarged left auricle. The aortic knob is not visible in the anterior view and in the left oblique position the aortic window is obscured by the large pulmonary vessels. The appearances are those of atrial septal defect. There is scoliosis of the dorsal spine."

The patient is active in her movements and walks very smartly without dyspnœa or visible increase in cyanosis; but she says that if she tries to walk any distance she becomes breathless. When she reported back in September, 1942, she had a harsh brassy cough and hoarseness, which suggested the possibility of a recurrent laryngeal nerve paralysis; but laryngoscopic examination (Dr. T. O. Howie) showed a simple laryngitis with congestion of the cords, and no evidence of paralysis.

Discussion

There can be little doubt, in the first place, that this patient's heart block is congenital, and in the second place that she has an atrial septal defect. The ventricular rate of 46 points to a congenital as opposed to an acquired block; the ventricular complexes resembling those found in dextrocardia are equally suggestive of a congenital lesion. The increasing cyanosis in later life and the gross distension of the pulmonary artery and its main branches without congestion of the periphery of the lung fields are features described by Bedford, Papp, and Parkinson (1941), as characteristics of atrial septal defect.

There is one respect in which the skiagrams of the present case differ from those published by Bedford, Papp, and Parkinson in their series, and from those of two cases of atrial septal defect seen by the author. Prominence of the conus in the antero-posterior view is a usual feature in cases of *A.S.D.*, but is absent in the present case. The contour of this patient's heart in the antero-posterior view resembles that of a case of ventricular septal defect with congenital block published by Stein and Uhr (1942); their case, however, lacks the distension of the pulmonary artery branches. Gross enlargement of the pulmonary artery is stated by Bedford, Papp, and Parkinson to be most exceptional in isolated ventricular septal defect; and they report that bulging of the pulmonary arc was absent in one of their cases of *A.S.D.*, which showed a rounded left border, while another showed a straight left border comparable with that of mitral stenosis.

FIG. 2.—Teleradiogram in antero-posterior position, showing enlargement of the heart and of the pulmonary artery.

FIG. 3.—Teleradiogram in right anterior (I) oblique position, showing a large pulmonary artery and backward displacement from a large left auricle.

FIG. 4.—Teleradiogram in left anterior (II) oblique position, with the aortic window obscured by the large pulmonary vessels.

The cause of the block in this case is thought to be a concomitant ventricular septal defect. The combination of atrial septal defect with ventricular septal defect is not uncommon; and although complete block is rare with atrial septal defect (it was present in none of Bedford, Papp, and Parkinson's cases) it has been described (Taussig *et al.*, 1938). The diagnosis of ventricular septal defect was, in fact, suggested at the time of her admission to hospital in 1934 on the grounds of the character of the murmur and the electrocardiographic findings.

The absence of the characteristic " bruit de Roger " at the present time could be explained in two ways. First, a fall in pressure in the left ventricle with a rise in right ventricular pressure may have equalized the pressure on the two sides with consequent disappearance of the murmur. Alternatively, its disappearance may have been brought about by rotation. Bedford, Papp, and Parkinson have shown that in *A.S.D.* there is progressive enlargement of the right ventricle which comes to form the apex and displaces the left ventricle backwards; rotation of the ventricles in this direction might well displace the murmur of a ventricular septal defect towards the left, that is to say towards the apex, where a systolic murmur is still audible in the present case.

The electrocardiographic features are curious; while the auricular complexes are upright in all leads, all deflections of the ventricular complexes are inverted in lead I. The ventricular complexes (but not the auricular complexes) are identical with those found in dextrocardia. The only other condition in which inversion of TI may be associated with an apparent right axial deviation is the QTI type of coronary thrombosis, a possibility that does not arise in this case. Apart from the conditions mentioned, I have never seen TI inversion resulting from simple right axial deviation without inversion of TII and TIII. Bedford, Papp, and Parkinson, however, record it in two of their cases of *A.S.D.* It is suggested that this feature of the cardiogram may also be due to rotation; with sufficient enlargement of the right ventricle towards the left and consequent displacement of the left ventricle backwards and towards the right, the interventricular septum will also be rotated clockwise; a ventricular electrocardiogram resembling that of dextrocardia might well be produced in this manner.

Summary

A case of atrial septal defect with ventricular septal defect and congenital complete heart block is described and discussed. She had fairly good health until she was 40, and was still working as a housekeeper at 46 years of age.

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CONGENITAL COMPLETE HEART BLOCK

BY

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From Guy's Hospital and the National Hospital for Diseases of the Heart

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Few of the reported cases of congenital complete heart block have been over twenty years of age. It seems, therefore, worth reporting seven cases who are in good health at various ages between 22 and 42 years. This ætiological factor should, therefore, be thought of in middle-aged and even in elderly patients with complete heart block of unknown ætiology.

Campbell and Suzman (1934), reporting eight cases, suggested that " when patients have been followed for a longer time they may be found in good health at a more advanced age." Of the eight cases reported in 1934, one had died and one was then only 3 so would still be a child; the remaining six, who were then between 12 and 33 years of age, and another man of 29, who was seen soon after, have been followed up; all have been traced and found to be leading ordinary lives without trouble from their hearts. This paper is not concerned with a clinical description of their condition which has been given already. It is an attempt to assess their capacity for leading a normal active life during the nine years that have elapsed since they were reported. The first six are given the same case numbers as in the previous paper; the seventh (Case 9) has not been reported previously.

Case 2. The diagnosis was made when she was 1 year old. She was under observation at the Heart Hospital from the age of 12 to 19 years. She was then a fit normal-looking girl, free from symptoms, and working as a shorthand typist. Her heart was a little enlarged and she was thought to have a patent interventricular septum.

Four years later she was examined at a routine visit and the condition of her heart was unchanged. A year later she had pleurisy; she did not feel ill for long and had little cough, but after some weeks' observation was diagnosed as early tuberculosis of the lung. She was in bed for two months and off work for six months, and six months later (with medical approval) married. This was shortly before the war. Since then, except that she has been " bombed out " of her home, she has led an uneventful life and kept in good health.

She is now 28 and does her normal household duties and feels less tired than when she was doing regular office work. She states that she cannot do heavy work without feeling unduly tired, but this has always been the case; recently to the surprise of herself and her friends she has been able to do all the heavier work connected with re-starting her London home.

Case 3. The diagnosis was made when he was 2, and confirmed at his school medical examination at 6 years old. He was under observation at the Heart Hospital at the age of 12 years. He was leading a normal life except that he had not been allowed to play games at school. The heart was just enlarged, and he was thought to have a slight interventricular septal defect.

After school he worked as an electrician and kept in good health. Though he did not play football, he did a good deal of camping and swimming.

He is now 22, and has been 2 years in the R.A.F. He actually passed for flying duties, but has continued his ground duties as an electrician. He has not been to hospital and has had nothing except very minor ailments.

Examined recently while on leave, he looked fit. His heart rate was unchanged at 48, and his B.P. 130/85. The systolic murmur was not very obvious and I was less sure of the diagnosis of patent interventricular septum. The apex beat was forcible and just out to the left. Radioscopy showed a large left ventricle with a very forcible beat and some prominence of the pulmonary conus. In proportion, his heart had certainly not become larger—the maximum transverse diameter in 1932 being 10·9 cm. in a chest of 20·4 cm.; and in 1942, 11·6 cm. in a chest of over 23 cm., which is some evidence, I think, that his work has not been too strenuous. He said he was a little breathless when there was specially heavy work, but was otherwise able to do everything in the same way as the others.

Case 4. Here, too, the diagnosis was made at the age of 2 years, and he was the only patient in the series with a clear history of Stokes-Adams attacks, frequently from the age of 2 to 4 and occasionally up to 8. He then got on well and was under observation at Guy's Hospital from the age of

12 to 16 years. His heart was slightly enlarged, the rate was generally about 42, and there were signs of a patent interventricular septum.

His story since his case was last reported is as follows. He started work at 16 as a baker's van boy, and though the work was light, the Stokes-Adams attacks recurred after a year. He took as much rest as he could without reporting sick, and changed his work to a hairdresser's apprentice. Here he kept quite fit for a year and gradually resumed cricket, football, and swimming. He then, at 18, started work in a garage and though it was heavy work felt very fit and got on well. At 21 (1938) he went into an aircraft factory and also indulged in cycling, dancing, and gymnastics, and had almost forgotten that there was anything the matter with his heart till long hours and hard work after the war had started made him feel it again. In spite of this he carried on and joined the Home Guard and acted as a fire watcher in his factory until January, 1941, when he again had a recurrence of his Stokes-Adams attacks. He took three weeks' rest in bed, again asking no medical advice, and changed his work, becoming a machine shop foreman where he managed well and had no further attacks (September, 1942).

He is now 25 and has done extremely well, working hard in many jobs and playing cricket and football, and since the war taking his full share in the Home Guard, firewatching, etc. He has without doubt done much more than he should, and I have advised him to take his heavier duties as easily as possible. I have given this story fully, because so often it is lack of courage rather than bodily disability that is responsible for the refusal to work hard and to face difficulties.

Case 5. Here, too, the diagnosis was first made at the age of 2 years. She attended the Heart Hospital for six months when she was 27 years old and, until that time, had easily been able to cycle 40 miles a day. Her heart was a little enlarged, the rate was from 46 to 50, and there were signs of a patent interventricular septum. Six years later, when she was 33, she was doing ordinary housework on a farm and was also walking two miles a day to her work without any real discomfort.

She is now 42 and writes that she has kept well and continued the same work, and that she has needed no medical attention of any sort for the last 15 years (August, 1942). So far as I am aware, this and the patient of Peel (1943) are the oldest cases of congenital complete heart block reported.

Case 7. The diagnosis was first made when she was 5 years old. She attended the Heart Hospital from the age of 20 to 22 years. She looked a very healthy girl and was leading a normal quiet life working as a hairdresser. She had never been allowed to play games and was somewhat short of breath on any special exertion. She came to hospital because of tiredness and of feeling faint and giddy, but there was nothing to suggest that she had Stokes-Adams attacks, and ordinary attacks of faintness were actually observed. The heart was full size and she was thought to have a defect of the interventricular septum.

She is now 31 and writes: "I have not been engaged in any regular occupation for several years with the exception of light household duties. But since the war I have been doing sedentary work with an optical firm and I have managed this all right, though at times it makes me tired. Apart from an occasional visit to my own doctor I have had no treatment for nine years."

Case 8. The diagnosis was first made when he was 13 years. He was under observation at Guy's

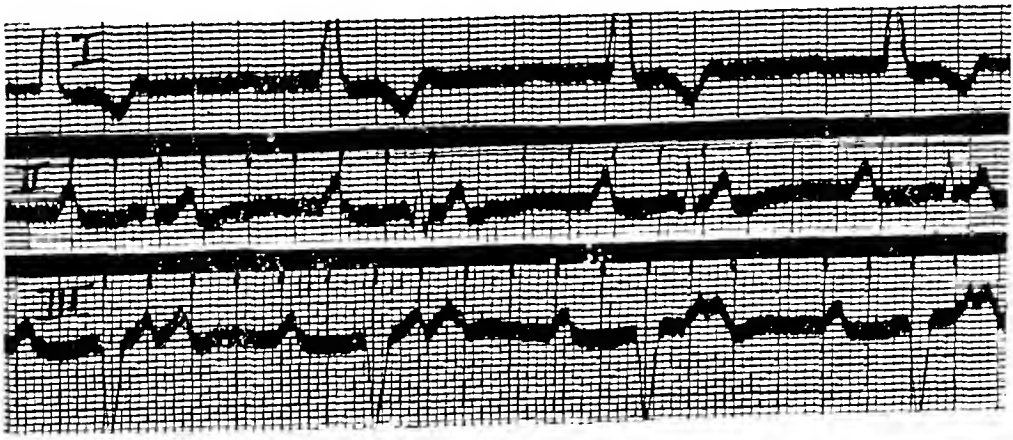

FIG. 1.—Case 8. The degree of heart block is probably complete, but it has the appearance of 2 : 1 block—a condition that is rare, if not unknown, in congenital cases—because the auricle is beating almost exactly twice as fast as the ventricle. The inversion of T in lead I has developed in the last ten years.

Hospital from then to 17 years, and felt well and was working in a bottling factory. His heart was slightly enlarged and he was thought to have a slight defect of the interventricular septum.

He was difficult to trace since the area in which he had lived was a waste of rubble as a result of enemy action. But by a curious coincidence he was attending Guy's Hospital at the time of this survey with a Colles' fracture sustained at work at Salisbury; he thought so little of his heart that he had not mentioned it at all.

He is now 26 and, though he was rejected from the army, has worked as hard as his mates, laying concrete floors for 54 hours a week, has played football in his club team, and has won several boxing matches. He has been regularly at work without medical attention for 9 years.

I have not been able to examine him, but have obtained a cardiogram which is shown (Fig. 1), because the signs of left ventricular preponderance with inversion of T in lead I, this last having developed since 1932 (see Fig. 13, *loc. cit.*), might suggest that it was associated with coronary atheroma or high blood pressure and not congenital; and also because it is suggestive of 2 : 1 heart block—a condition which I have not seen with congenital disease.

Case 9. *Not previously reported.* A dental surgeon, aged 29, came to see me in 1935 because his slow heart rate had led to difficulties about life insurance. His only recent illness had been a rather severe attack of migraine six months before, with vomiting, faintness, and hemianopia; he had reduced his cigarette smoking and there had been no recurrence.

His heart rate was generally between 36 and 42 and the electrocardiogram confirmed complete

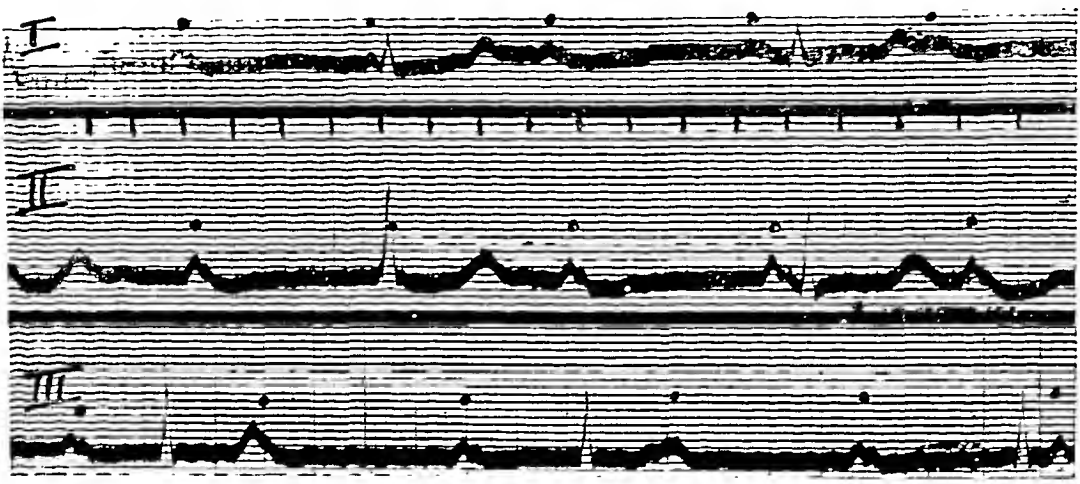

FIG. 2.—Case 9. Congenital complete heart block in a man of 29 with few symptoms. Auricular rate 80; ventricular rate 36; this could easily be increased to 50 after exercise.

heart block without any other abnormality. The heart was full-sized or a little enlarged to the left (max. trans. diam. 11·5 cm. in a chest of 21·5 cm.) with a rounded left ventricle. There was a systolic murmur, loudest half-way between the apex and the mid-line, which was thought to indicate a patent interventricular septum, though it was softer than in most such cases. The blood pressure was 125/80 and no other abnormality was found. The heart rate quickened a little with exercise, rising from 18 in the half-minute before to 27 and 23 in the first two half-minutes after a simple stepping exercise (18 steps a minute for 3 minutes).

The diagnosis of complete heart block had not been made at an early age so as to make it certain that this was congenital, but there was no history of rheumatism or diphtheria or of other serious illness, and he had seen Dr. R. O. Moon in early childhood because there was some question about his heart being enlarged. His mother remembered the heart was then said to be slow and that the doctors always seemed very interested. Dr. Moon wrote that he had never found anything to suggest rheumatic or other inflammatory disease and that after keeping him under observation for some time he had allowed him to ignore it, and that he thought the diagnosis now made was probably correct, though he had no notes available to confirm the actual rate of the pulse.

I advised that he should lead a normal life and that he should be accepted for life assurance with a small extra. It is interesting that as a student at Guy's he remembered being admitted to hospital with jaundice and being demonstrated as a case of bradycardia due to this, showing how readily congenital heart block may be overlooked.

He is now 36 years of age, feels quite fit and leads a normal life, practising as a dentist, cycling (since the war), and gardening. His pulse rate is generally between 35 and 40.

One other new case, though not of interest from the present point of view, may be mentioned because of the post-mortem finding of a patent foramen ovale without any patency of the interventricular septum.

Case 10. A girl, aged 8 months, was admitted under Dr. E. C. Warner for severe malnutrition. She was short of breath, even feeding, and the heart was enlarged, with the rate between 48 and 60. A diagnosis of congenital complete heart block was made and she was sent to see me. The diagnosis was confirmed by a cardiogram (auricle, 114; ventricle, 44), which was normal otherwise. There was thought to be a patent septum on the evidence of a systolic murmur.

She died a few weeks later and Dr. Warner wrote that the heart was much enlarged with collapse of the left upper lobe of the lung. There was a large patent foramen ovale, but no visible abnormality in the interventricular septum or elsewhere in the heart, which unfortunately was not kept.

Probably, some of the elderly patients with complete heart block of unknown ætiology are in fact congenital cases that have not been recognized, partly because the pulse is generally not nearly as slow as with acquired heart block. The following case might perhaps be of this nature though the evidence is very incomplete.

She was first seen by me when she was 65, with symptoms of intestinal obstruction. She had led a semi-invalid life for 20 years. She had no cardiac symptoms, but the heart rate was 40 due to complete heart block. There were no murmurs, no rise of blood pressure (130/80), no more arterial thickening than might be expected at her age, and only slight enlargement of the heart to the left.

Twenty years before she had an unfortunate partial colectomy, followed two years later by an operation for partial obstruction and subsequently by two attacks of intestinal obstruction due to volvulus. Her weight was 4 st. 9 lb. and had not been above 6 st. since the first operation. She was relieved of this attack but died a year later with intestinal obstruction.

Her doctor wrote that during the 7 years he had known her the heart rate had always been slow, and that he thought it had always been slow as all the doctors for the past 20 years had remarked on it. He also reported that one of her brothers had a slow pulse.

This history only takes her heart block back till she was 45, but as it was symptomless and found by chance it may well have been there before, for if it had been due to coronary disease something more would probably have been found after 20 years. The rate of 40 is slower than in many congenital cases, but the idiopathic ventricular rate may perhaps become slower as the patient gets older.

Summary and Conclusions

The present condition of seven cases of congenital complete heart block, now aged 42, 36, 31, 28, 26, 25, and 22 is reported shortly. Full details about six of them were published nine years ago. All these six and one other (first seen shortly after the paper was published) have been traced—a very satisfactory result after this interval of nine years, especially in war time.

All are alive and well, and their degree of activity could be taken as a fair cross section of the general public. Of the four men, two are working men, who though rejected from the army have led strenuous lives, both in their work and in their play—almost certainly doing more than they ought to as their hearts are not normal. One has been two years in the R.A.F. and has been passed for flying duties, and the fourth is a professional man who leads a normal life with gardening and cycling in his spare time.

Of the three women the eldest does ordinary housework on a farm, but the other two lead rather more sheltered lives, possibly because their doctors have discouraged them too much. One was at easy work till she developed tuberculosis a year before her marriage, and the other after doing light duties at home for six years has taken up sedentary work since the war. Except for the one case of tuberculosis, no unexpected developments have arisen in any case, and the one who had Stokes-Adams attacks in infancy has led the most strenuous life with only two short periods of recurrences.

Congenital complete heart block is not rare. It is overlooked because the rate is relatively fast, about 40–56, and also because the possibility is not remembered.

If there are no special complications carrying special risks of their own, the prognosis is good, and it will probably prove that the condition is compatible with survival to old age.

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TUBERCULOUS PERICARDIAL EFFUSION

BY

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Tuberculous pericardial effusion is not common; and so the case described is of interest on account of the patient's age, the frequency with which the pericardial effusion required tapping, the relative absence of symptoms during most of the illness, and the stages through which the case passed from gross effusion to relative dryness at autopsy with only about 2 oz. of fluid in a greatly thickened pericardium.

Description of Case

A sailor, aged 23, was admitted into a hospital on August 16, 1940, for epigastric pain and frequent vomiting, which had begun three days previously. There had been a similar attack three months previously. There was continued pyrexia up to 102. The diagnosis was apparently difficult until he complained of some sub-sternal tightness a few days later, when attention was directed to his heart. This was found to be enlarged, 1 inch outside the nipple line, but it was only after an X-ray that the diagnosis of pericardial effusion was established. Before this, on account of dullness at the left base of the lung with diminished breath sounds, a pleural effusion was suspected, but the X-ray did not confirm this. The blood pressure was typically low, 100/70.

Repeated tappings were performed as under:

August 23, 300 c.c. ; *August* 27, 400 c.c.; *August* 30, 500 c.c.; the fluid each time being sterile and clear and straw-coloured; *September* 6, 300 c.c.; and *September* 13, 550 c.c., the fluid being deeply blood-stained on these two occasions. (For later tappings see below.)

On Sept. 16 he was admitted to the Southern Hospital, where he came under my observation. The heart was greatly enlarged, both to left and right. The heart sounds were faint and muffled. Continued pyrexia was still present, varying between 99 and 103. Symptoms were absent, except for sub-sternal tightness which he seemed to experience whenever the effusion increased; this was relieved after tapping. Tachycardia was a constant feature throughout, the pulse rate being about 100 to 120. The blood sedimentation rate was 78 mm. after one hour. Blood culture was sterile. A Mantoux test (1 in 10,000) was negative. And in spite of a negative guinea-pig test on two occasions, the diagnosis of tuberculous pericardial disease was made.

September 24, aspiration of 520 c.c. of old blood-stained fluid. There was no change in his blood pressure, 105/80, before and after, or in the cardiogram which showed the characteristic T wave inversions.

November 6, aspiration of 600 c.c. of fluid, less blood-stained. He had remained fairly comfortable and without sternal pain. On this occasion an air replacement was done, and an X-ray afterwards showed the parietal layer of the pericardium, which measured half an inch thick. The cardiac shadow was not diminished after the tapping. X-ray on December 10, showed the air replacement to be absorbed, and an increase in the size of the effusion. A course of sulphapyridine (17 g.) was given about this stage, and brought down the temperature for a time. Towards the end of December he developed a dry cough and the temperature rose again to 102. He began losing weight and he had night sweats.

December 28, aspiration of 600 c.c. of amber-coloured fluid ; air replacement of 100 c.c. Fine crepitations were now heard, and an additional diagnosis of miliary tuberculosis of the lungs was made. He gradually became worse about the middle of January 1941, and was mildly delusional at times. On January 19, 1941, he became drowsy; coma set in and he died the next day.

Post-mortem examination. Pleura: light fibrous adhesions, obliterating both pleuræ.

Heart: Great dilatation of the pericardial sac, which contained only 2 oz. of amber fluid, but was much thickened by granulomatous tissue. A layer of friable yellow fibrin, uniting the thickened layers of the pericardium, up to 1 cm. thick; no loculations. Heart itself only slightly enlarged; valves normal.

FIG. 1.—Radiogram of the heart showing much dilatation of the pericardial sac.

Lungs: Congested and closely studded with granulomatous miliary tubercles; no cavities. Caseous glands in both hila and at the bifurcation of the bronchi, two inches by one quarter inch in size on each side.

Liver: Cloudy swelling and a few miliary tubercles.

Spleen: Three times normal size; some tubercles.

Kidneys: Cloudy swelling with streaks of pus in the pyramids; studded with miliary tubercles.

Bladder: Infected with pus.

Prostate: Caseous tuberculosis present.

Brain: General œdema. Sero-meningitis over the base of the brain with a few scattered tubercles in the fissures. A tuberculoma, 0·5 cm. in diameter, in the left occipital cortex.

Histological examination confirmed tuberculosis.

Discussion of Case

There is no doubt that in this case the primary focus was a tuberculous gland in the mediastinum, secondarily affecting the pericardium. And later as the disease progressed, further dissemination occurred, causing generalised miliary tuberculosis. Another point of interest was the absence of lung symptoms until the final phase of his illness. Hæmorrhagic pericardial effusions are said to be characteristic of tuberculosis. I think this is an open question, and the probability of trauma when needling must be taken into full account. In this case the first three tappings were not blood-stained. The next two were deeply blood-stained, and the succeeding ones clearly pointed to the presence of old blood in the sac. The last specimen of pericardial fluid was only amber-coloured.

Another point of interest is that the cardiac shadow did not diminish after paracentesis, owing to the very thick and rigid pericardium.

FIG. 2.—Photograph of the heart showing much thickening of the pericardium.

The negative results of laboratory findings, such as the absence of tubercle bacilli in the fluids and the failure of inoculation of guinea pigs to produce any result, should also be stressed.

POST-MORTEM STATISTICS AT GUY'S HOSPITAL

To assess the incidence of tuberculous pericarditis I have analysed 1893 autopsies at Guy's Hospital from January 1935 to June 1939. There were 102 tuberculous cases with lung involvement. There were 6 cases of tuberculous pericarditis, confirmed by histological section; 2 others with pericarditis were most probably tuberculous, judging from the post-mortem description, but cannot be included as there was no mention of tuberculosis macroscopically or microscopically. There was also one case of myocardial tubercle alone, without pericardial involvement. This makes an incidence of 0·3 per cent of all the cases that came to autopsy during this period, and 6 per cent of all cases that had tuberculous involvement in any organ. If the two probable cases were included it would raise the incidence among general cases only to slightly over 0·4 per cent, but it would raise the incidence among tuberculous cases to as high as 8 per cent.

As a comparison for incidence, Kornblum, Bellet, and Ostrum (1933) give figures of 1 per cent among general cases and 4 per cent among tuberculous cases (Philadelphia Hospital) : they reported 17 cases during a period of two years. The incidence of tuberculous pericarditis among non-

Europeans in South Africa appears to be much greater than in the Guy's Hospital series; Heimann and Binder (1940) reported on 31 cases over a period of 14 years, which gives an average of over 3 cases a year. This contrasts with 1·3 cases a year at Guy's Hospital, and 8·5 cases a year at the Philadelphia Hospital. The number of autopsies is not mentioned in either instance.

Of the 6 cases, only one was diagnosed as such during life, the remainder being post-mortem findings. (The case described in this paper does not belong to this series.) In the remaining 5 the tuberculous pericarditis was a complication of some other disease. In all instances except in Case 3, the mediastinal glands were tuberculous.

Case 1. Male, aged 43. Myelogenous leukæmia. Post-mortem confirmation. Clusters of large yellow tubercles radiating outward to the hilar lymph glands which were caseous. Caseous nodules in lungs. Visceral and parietal layers of the pericardium covered by fibrinous exudate and studded with tubercles. Sac containing 300 c.c. of clear yellow fluid.

Case 2. Male, aged 70. Died on arrival at hospital from hæmorrhage from the lungs. No other clinical history.

Post-mortem: Lungs adherent to pleura. Surface extension of miliary follicles in the sub-pleural lymphatics. A reactivated Ghon focus in the left lower lobe. Mediastinal glands tuberculous. Pericardial sac thickened by recent lymphatic extension of the miliary type from the adjacent pleura. Light fibrous adhesions between both layers of the pericardium ; no exudate.

Case 3. Male, aged 56. Syphilitic aortic incompetence with pleural effusion. Died two months after admission from cardiac failure.

Post-mortem: In addition to the widened syphilitic aorta, a left-sided pleural effusion of clear fluid. Two loculated empyemas in the right pleural cavity, their walls consisting of tuberculous granulation tissue. External surface of the pericardium covered with a delicate fibrinous exudate. Both layers moderately adherent and covered by a thick yellow granular fibrino-purulent exudate. No evidence of any tuberculous lesion in the lungs. Mediastinal glands likewise not affected by tubercle.

Case 4. Female, aged 4 months. Admitted for meningitis.

Post-mortem: Miliary tuberculosis of all the organs. Mediastinal glands caseous, with a caseous focus in the right upper lobe of the lung. Pericardium, miliary tuberculosis; no effusion.

Case 5. Male, aged 23. In hospital for over two months, and treated for increasing cough, pain in the chest, and later for pleural effusion. Sputum always free from tubercle bacilli. Pericarditis one month before death. The patient gradually went downhill and died. Ten months previously he had begun to have symptoms of lassitude and anorexia.

Post-mortem: Right lung studded with miliary tubercles. A fibro-caseous empyema, only 2 or 3 weeks old, in the lower third of the right pleural cavity. On the left side a much older thick walled empyema. Mediastinal glands caseous. Pericardium universally adherent owing to tuberculous pericarditis of considerable duration, caseating freely. Heart not enlarged. A large caseating nodule attached to the free border of the marginal cusp of the mitral valve. Section showed that the pericarditis was of many weeks' duration.

Case 6. Male, aged 14. Admitted three months before death on account of cough, dyspnœa, cyanosis, and pleural and pericardial effusions. Both cavities tapped once; clear fluid drawn off containing many lymphocytes. Tuberculous pericardial effusion diagnosed clinically, and injection into a guinea pig confirmed this by producing a tuberculous lesion. Later on, headaches and meningitic symptoms, followed quickly by the patient's death.

Post-mortem: Bilateral pleural effusions containing clear fluid. Old and recent pleurisy on both sides. A great deal of sub-pleural miliary tubercle. No evidence of any tuberculous lesions in the lung substance. Mediastinal glands caseous. Pericardial sac enormously thickened, only slightly adherent to the lungs, and containing much granulation tissue; easily broken down adhesions between the two layers of the pericardium. Heart of very small size. Section showed that the disease process was of considerable age. This was the only one of the six cases that was diagnosed as having tuberculous pericarditis during life.

Discussion of Autopsies

An interesting fact brought out by the analysis of the 1893 cases was that of the 102 with tuberculosis there were 27 with an excess of pericardial fluid alone, without any macroscopic evidence of pericardial disease; the amounts varied from slight excess to 200 c.c. of fluid. I feel that if sections were examined in these cases there would be microscopic evidence of miliary tubercle of the peri-

cardium. Obviously this point is of academic rather than of practical interest as all these 27 cases died from their primary tuberculous lesions. Thus 26 per cent of the tuberculous cases had some excess of pericardial fluid. A comparison with 202 consecutive autopsies was made as to the frequency of excess pericardial fluid in 41 primary cardiac cases; 13 had excess of fluid (32 per cent). There were also 13 tuberculous cases in this small series, 3 of which had excess of fluid, the proportion happening to agree well with the 1893 cases which were analysed.

Of these 41 cardiac cases, 10 had rheumatic valvular disease and 12 had high blood pressure. 5 of the 10 in the rheumatic group (50 per cent) had excess pericardial fluid and 4 of the 12 (33 per cent) in the hypertensive group had excess fluid.

In the 1893 autopsies, only 14 cases of hæmopericardium occurred, and of these 14 cases only 1 was of tuberculous pathology. In this one the epididymis, prostrate, meninges, and lungs were affected; there was nearly 4 oz. of bloody fluid in the sac; the pericardium was normal to naked eye, but it was not sectioned. The remainder consisted of 8 cases of rupture of the myocardium following cardiac infarction ; 1 case of rupture of a dissecting aortic aneurysm, 3 cases of carcinomatosis, and 1 case of high blood pressure with a cerebral hæmorrhage.

Summary

A case of tuberculous pericarditis is described. It is suggested that in any obscure case of pericardial effusion, especially where this is large, tuberculosis should be thought of as a possible diagnosis; and that this is still more likely if tapping has to be repeated.

Among 1893 consecutive autopsies there were 6 cases of tuberculous pericarditis, but only one of these had been diagnosed clinically. Hæmopericardium did not occur in any of these cases. Some excess of pericardial fluid was found in about a quarter of all the tuberculous cases.

I would like to thank Dr. Willis for his kindness in performing some of the pericardial tappings, and Dr. Alan Daly for his permission to publish this case.

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SIGNS SIMULATING THOSE OF MITRAL STENOSIS

BY

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Duplication of the second heart sound at the apex, especially when this is associated with a systolic murmur, is apt to be regarded by recruiting medical boards as evidence of an organic mitral lesion. The purpose of this paper is to suggest that this sign is physiological, and to put forward a hypothesis to account for it and for certain other signs that are apt to lead to a mistaken diagnosis of mitral stenosis. In a group of 835 recruits referred to the writer by medical boards of the Ministry of Labour and National Service, a duplicated second heart sound at the apex was heard in 157; this series does not include any case in which an early diastolic murmur would be heard or a presystolic murmur could be elicited by exercise.

The duplicated second sound, like the presystolic murmur of mitral stenosis, is best heard with the patient lying on his left side. As it seemed probable that this was due to the change in the axis of the mitral orifice with change of posture, the writer sought the help of Professor Wood Jones, who kindly examined a series of cadavers hardened in formalin and found that, relative to the long axis of the body, the blood stream issuing through the mitral orifice was directed mainly forwards with an inclination of about 20° downwards and slightly towards the left. Thus, with the patient lying on his back, the blood stream is flowing almost directly against gravity, whereas when he turns on his left side it is flowing horizontally. The latter position would tend to accelerate the blood flow from auricle to ventricle, and so, as will be shown later, would render conditions more favourable for duplication of the second heart sound.

The second element of the duplicated second heart sound follows the closure of the semilunar valves by about 0·1 sec. It therefore corresponds in time to the physiological third heart sound; in fact the two appear to be identical. Thayer (1908) found that a third heart sound could be heard in 65 per cent of healthy young persons. He also demonstrated, experimentally in dogs, a similar sound which corresponded in time to the sudden distension of the ventricle that occurs early in diastole, and he suggested that the third heart sound was due to sudden tension of the A-V valves produced by the first rush of blood from auricle to ventricle.

The physiological third heart sound is much more commonly heard in young than in older subjects. The same is true of the duplicated second sound in recruits. Table I gives the age incidence of the 157 cases in the present series as compared with the age incidence of the whole group of 835 cases among which they occurred.

TABLE I

AGE INCIDENCE OF DUPLICATED SECOND SOUND

Age	Whole group	With duplicated second sound	
		Number	Percentage
Under 20	228	96	43
Over 20	604	61	10
20–24	84	13	14
25–29	151	20	13
30–34	164	17	10
35–39	136	10	7
Over 39	69	1	1
Not stated	3		
Total	835	157	19

From this table it will be seen that whereas the incidence was 19 per cent in the whole group, it was 43 per cent in men under twenty as compared with only 10 per cent in men over that age.

Most of these young men appeared to be perfectly fit; some were athletic and many were well above average physique. In the opinion of the writer, 70 per cent were fit for Grade I, and of the 46 cases placed in lower categories, 22 were lads of eighteen or nineteen whose physical development was in arrear of their age. They were accordingly temporarily placed in Grade II or III. Thirteen only were down-graded on account of permanently poor physique, and 11 for other reasons.

So far as pulse rate and systolic blood pressure are concerned there was remarkably little difference between recruits with a duplicated second sound and the entire group of which they formed part. In both cases the mode for the systolic pressure was 130–140. Only 10 per cent of the recruits with a duplicated second sound, however, had a diastolic pressure over 80 as compared with 22 per cent in the entire group. This is not unexpected in view of the lower average age in the former group.

Only a few of the electrocardiograms exhibited right axis deviation, but in most cases radioscopy did suggest that in men with a duplicated second heart sound the pulmonary arc was more prominent than usual, the heart conforming to the childish contour. William Evans (1942), whose observations were based on actual measurments, came to the same conclusion.

In these recruits, the duplicated second sound is generally associated either with a frank apical systolic murmur or with an impure first heart sound; often it was this murmur which was responsible for the case being referred for a second opinion. It seems possible that this murmur is attributable to a safety-valve mitral incompetence, associated with overfilling of the ventricle, and is comparable to the murmur which one hears in normal people immediately after severe physical exertion.

The Presystolic Murmur

In endeavouring to assess the significance of the duplicated second heart sound and to determine the mode of its production, it is helpful to consider the incidence of the crescendo presystolic murmur of mitral stenosis. In the production of an obstructive murmur two factors are concerned, the size of the orifice and the velocity of the blood flow: the one is static, the other dynamic. No matter how small the orifice, a murmur will only be produced when the blood flowing through it attains a certain critical velocity. The importance of the dynamic factor is well illustrated by following patients with mitral stenosis through pregnancy. In many of these cases, a loud presystolic murmur is heard during the later months of pregnancy: but, after delivery, no murmur is audible at rest, though one can be elicited by exercise. In such cases, it is obvious that the presence or absence of a murmur is determined not by the size of the mitral orifice but by the velocity of the blood flow.

There is an inverse mathematical relation between the degree of stenosis and the velocity of the blood flow required to produce an obstructive murmur. When stenosis is considerable a murmur is heard at rest, but when it is trivial there is no murmur unless the rate of blood flow is increased by exercise. The following observations suggest that even when the mitral orifice is normal, an obstructive murmur may be produced if the rate of blood flow be sufficiently increased.

In the course of a routine examination of athletes at the Olympic Games in Amsterdam, Ellis and the writer (1931) found that, in certain perfectly normal subjects, the first heart sound might be so modified that it was indistinguishable from the presystolic murmur and accentuated first heart sound of mitral stenosis. This sign was present in 12 out of 192 athletes examined; three were Marathon runners, three long-distance runners, and three long-distance cyclists—all athletes whose particular form of sport entailed prolonged and severe exertion. It was not present in any of the 18 sprinters or 16 middle-distance runners included in this series. A similar observation was made by Sewall (1909), twenty years previously. His explanation was that when the ventricle is filled at a certain rate, the reflux of the blood current tends to bring the cusps of the mitral valve into approximation, so that the auricle, in expelling its contents, has to force a channel between them. This explanation is analogous to the Austin Flint hypothesis, but it seems unduly speculative. An alternative explanation is that, in athletes who indulge in prolonged and severe exertion, the auricles share in the general cardiac hypertrophy that is known to occur. Consequently the velocity with which the blood is projected into the ventricles by the hypertrophied auricles is greater than under normal conditions, and the mitral orifice proves relatively too small for the increased rate of blood flow.

Further evidence in support of this hypothesis is derived from the fact that in many cases of acute thyrotoxicosis the first heart sound bears a distinct resemblance to that of mitral stenosis. In 1914 Bridgeman demonstrated in graphic records of the normal first heart sound a series of small vibrations synchronous with auricular systole. These were of such low intensity that they failed to reach the threshold of audibility. Amplification of these presystolic vibrations, sufficient to render them audible, accounts for the roughening of the first heart sound in thyrotoxicosis (Bramwell, 1935). A

similar modification of the first heart sound is liable to occur in any excitable overacting heart and may lead to a mistaken diagnosis of mitral stenosis. This mistake is not surprising; for, if the hypothesis outlined above be correct, there is no auditory line of demarcation between anatomical stenosis due to a narrowed orifice and physiological stenosis due to an increased rate of blood flow. The one is absolute; the other, relative.

The Early Diastolic Murmur

To revert to consideration of the significance of the duplicated second heart sound at the apex, the diastolic part of the heart cycle may be divided physiologically into three phases in accordance with the velocity of the blood flow from auricle to ventricle. When the mitral valve opens, the pressure in the auricle is much higher than in the ventricle, and the blood which had been accumulating behind the closed valve during systole rushes in a swirling torrent into the empty ventricle. As soon as the initial difference in pressure between the two chambers has been relieved, the rate of blood flow from auricle to ventricle diminishes and the torrent is converted into a quietly flowing stream. Finally, when the auricle contracts, the rate of blood flow through the mitral orifice is again increased.

In extreme stenosis a rumbling murmur is heard throughout diastole, but in slight stenosis it is only during early diastole and presystole that the velocity of blood flow is sufficient to produce a murmur, the intermediate phase of diastasis being silent.

The fact that, in the lesser degrees of mitral stenosis, a presystolic is more common than an early diastolic murmur suggests that the difference in pressure on the two sides of the mitral orifice is greater during auricular systole than during early diastole. This may be due to the fact that in old-standing cases of mitral stenosis, left auricular hypertrophy is the rule, and the force with which the blood is ejected by the auricle is correspondingly increased.

The classical signs of slight mitral stenosis are a presystolic murmur with an accentuated first and a duplicated second heart sound. When stenosis is more pronounced the duplicated second sound is followed by a diastolic murmur, the duration of which varies with the degree of stenosis.

The second element of the duplicated second sound in mitral stenosis is called by French cardiologists " le claquement d'ouverture de la mitrale " and ascribed to vibrations of the thickened mitral valve set up by the first rush of blood from auricle to ventricle. In this respect its mode of production is similar to that of the normal third heart sound, but in the one case the sound is attributable to the stenosis of the mitral orifice and the thickening of the mitral cusps, whereas in the other the orifice and valves are normal but the rate of blood flow is increased. The former is the pathological, the latter the physiological, third heart sound.

Summary

In a consecutive series of 835 recruits, a duplicated second heart sound (generally associated with an apical systolic murmur) was present in 157 cases.

The duplicated second heart sound was best heard when the patient lay on his left side; the reason for this is discussed. Duplication of the second heart sound was much more common in men under 20 than in older recruits. Seventy per cent of the men in whom it was present were considered fit for Grade I. Radioscopy in these cases generally showed an increased prominence of the pulmonary arc.

Since the production of an obstructive murmur depends on the degree of obstruction *relative* to the velocity of the blood current, it is suggested that an increased rate of blood flow through a normal mitral orifice may be instrumental in producing: (*a*) the accentuation and roughening of the first heart sound heard in certain athletes, in thyrotoxicosis, and in other conditions in which the heart is overacting, and (*b*) the duplicated second heart sound heard in healthy subjects. Both these signs are therefore regarded as signifying a " relative " mitral stenosis.

This hypothesis entails a physiological conception of mitral stenosis based on the volume of blood which an orifice of a certain size can transmit in unit time.

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ELECTROCARDIOGRAPHIC PATTERNS OF COMBINED VENTRICULAR STRAIN

BY

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The characteristic electrocardiographic patterns of right and left ventricular strain have been recognized for some time. While originally deviation of the electrical axis, reflected in the direction of QRS in the limb leads, was taken to indicate ventricular hypertrophy (4, 5, 7, 9–12, 16, 23–35, 28, 29, 37, & 38), later studies showed that the S–T–T pattern (1, 8, 22, 26, 27, 30, 31, 33, & 41) presented the more reliable evidence of chronic ventricular strain and was indicative of ventricular hypertrophy even in the absence of deviation of the electrical axis (2, 19). Experience in recent years has shown that the use of multiple chest leads is imperative in distinguishing between records of left ventricular strain and those of myocardial infarction involving the anterior wall (3, 13, 14, 15, 17, 20, 32, & 40). It has been shown (6, 16, 21, & 24) that the patterns of chronic ventricular strain do not necessarily indicate unilateral ventricular hypertrophy, but more often indicate the site of preponderant hypertrophy, or what is equivalent, the site of greater ventricular strain. The occurrence of cardiograms presenting a combination of features characteristic of both right and left ventricular strain suggested to us that bilateral ventricular strain might be reflected on occasion in the cardiogram. We therefore undertook to analyse the various possible patterns suggestive of combined strain and to correlate them with the clinical and autopsy data.

The cases for this study were selected at random from the files of the Heart Station of the past few years. Records showing evidence of myocardial infarction, acute cor pulmonale, or digitalis effect were discarded, because these conditions are known to imitate right and left ventricular preponderance in the absence of demonstrable ventricular hypertrophy or to mask the true pattern when hypertrophy is present (18, 21). It has also been shown (18) that these conditions may imitate the changes indicative of combined ventricular strain. A total of 47 records (some previously reported) were found and form the basis of this study. They were readily subdivided into 6 patterns (see Table I and Figs. 1 to 4) as follows :

TABLE I

DESCRIPTION AND FREQUENCY OF THE VARIOUS PATTERNS OF COMBINED VENTRICULAR STRAIN IN 47 CASES

Type	Electrocardiographic Pattern	Number of Cases	Clinical or Autopsy Evidence of Combined Ventricular Strain	Figure
I.	QRS contour of right ventricular preponderance combined with the S–T–T contour of left ventricular preponderance.	6	6	Fig. I, B and C
II.	QRS contour of left ventricular preponderance combined with the S–T–T contour of right ventricular preponderance	1	1	Fig. 2 C
III.	Concordant pattern of left ventricular preponderance (QRS upright in the limb leads with S–T–T abnormalities)	11	8	Fig. 3 A
IV.	Concordant inverted pattern of heart strain (QRS inversion in all three limb leads without any Q waves present)	7	7	Fig. 3 B
V.	Prominent S waves in all the limb leads with the major QRS deflection upward in at least two leads (S-T–T abnormal)	3	3	Fig. 3 C
VI.	Small upright QRS_1 or equiphasic QRS_1 with an S_1, with deep S waves in leads II and III greater in size than the upward deflection of QRS_I in lead I.	18	12	Fig. 4 A
	One record not fitting into any of the above described patterns	1	1	Fig. 4 B
	Total number	47	38	

* Aided by the A. D. Nast Fund for Cardiovascular Research and the Nelson Morris Fund.

Type I. The combination of a QRS contour of right ventricular preponderance (QRS_1 mainly inverted, with an S wave, and QRS_3 upright) and an S–T–T contour of left ventricular preponderance ($S–T_1$ depressed and bowed upward, with T_1 inverted or diphasic). (Fig. 1, B and C)

Type II. The combination of a QRS contour of left ventricular preponderance (QRS_2 and QRS_3 inverted, with S waves) and an S–T–T contour of right ventricular preponderance ($S–T_2$ and $S–T_3$ depressed, with T_2 and T_3 inverted). (Fig. 2 C)

Type III. Concordant type of left heart strain (20) (QRS mainly upright in all limb leads, with $S–T_1$ and $S–T_2$ depressed, and with T_1 inverted or diphasic). (Fig. 3 A)

Type IV. Concordant inverted type of heart strain (20) (QRS mainly inverted in all limb leads, but without Q waves). (Fig. 3B)

Type V. Prominent S waves in all the limb leads, with either QRS_1 or QRS_3 mainly upright, associated with an abnormal S–T–T contour. (Fig. 3 C)

Type VI. Small upright or equiphasic QRS_1 (the latter with an S wave), with QRS_2 and QRS_3 mainly inverted, and with deep S waves larger than QRS_1. (Fig. 4 A)

One interesting case not fitting into any of the above categories will be described below. (Fig. 4 B)

In 81 per cent of the 47 cases selected, the cardiographic diagnosis of combined strain was substantiated by the clinical, radiological, and, when available, by the autopsy findings.

In most of the cases of the Type I pattern, serial records taken over a period of years were available, and the gradual evolution of this pattern could be followed (Fig. 1). All 6 were instances of old rheumatic mitral valvulitis; one showed in addition aortic valvular involvement, another showed

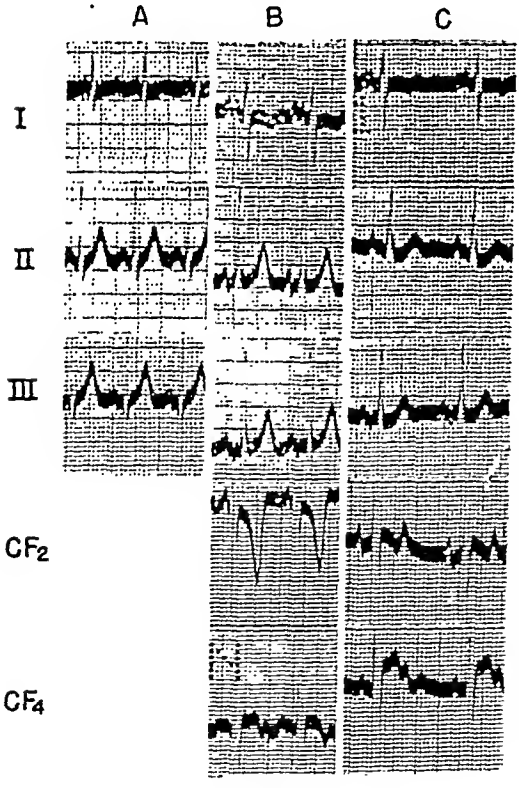

FIG. 1.

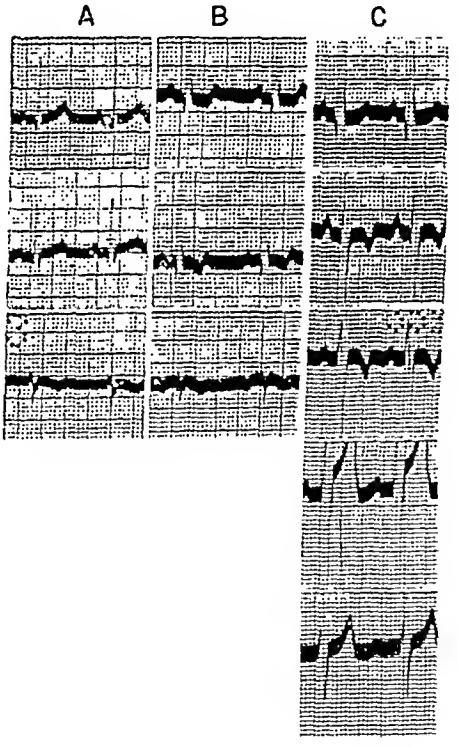

FIG. 2.

FIG. 1.—The development of the Type I pattern of combined ventricular strain in a patient with rheumatic mitral stenosis and insufficiency and aortic insufficiency. (A), taken at the age of 3, shows no axis deviation; (B) and (C), taken 3 and 4 years later, show a QRS pattern of right ventricular strain with an S–T–T pattern of left ventricular strain. Note the broad and notched "mitral" P waves.

FIG. 2.—The development of the Type II pattern of combined ventricular strain in a patient with rheumatic heart disease with mitral and aortic stenosis and insufficiency and a tricuspid lesion. (A), taken at the age of 14, shows a normal left axis shift. (B), taken 1 year later, shows an S–T–T contour in leads II and III which does not fit the contour of left ventricular preponderance of lead I. (C), taken 7 years later, shows a QRS contour of left ventricular preponderance with T inversion in leads II and III, characteristic of right ventricular preponderance. Note the progressive widening of QRS between (A), (B), and (C).

deformity of the other three valves, and a third showed marked pulmonary emphysema. In two of the six cases autopsy findings corroborated the clinical diagnoses and the bilateral ventricular enlargement.

Only one example of the Type II pattern was encountered. This boy, aged 21, had clinical evidence of severe rheumatic carditis with mitral and aortic stenosis and insufficiency and a probable tricuspid lesion. Numerous records taken over thirteen years showed progressive inversion of QRS in leads II and III with inversion of T in those leads (Fig. 2). Digitalis was never given to this patient.

Kaplan and Katz (1941) in their description of the so-called concordant pattern of left heart strain suggested that the absence of axis deviation might be due to concomitant right ventricular strain, either on the basis of episodes of left ventricular failure (36) or an associated lesion putting a strain primarily on the right ventricle. They collected 17 cases and showed that 4 were attributable to combined mitral and aortic lesions, 9 to hypertensive heart disease with previous episodes of left ventricular failure, 2 to syphilitic aortic insufficiency with failure, and in the remaining 2 only hypertension was evident with no previous congestive heart failure. In one of the latter, the absence of axis shift was attributed to a displacement of the heart and mediastinum to the right by a massive pleural effusion.

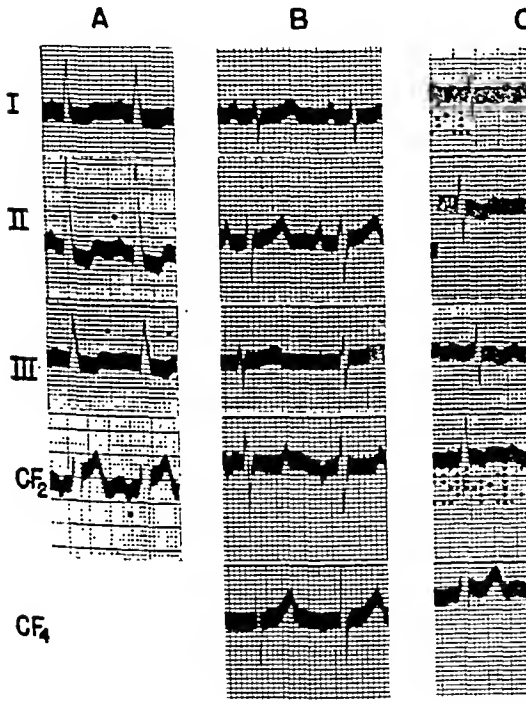

FIG. 3.

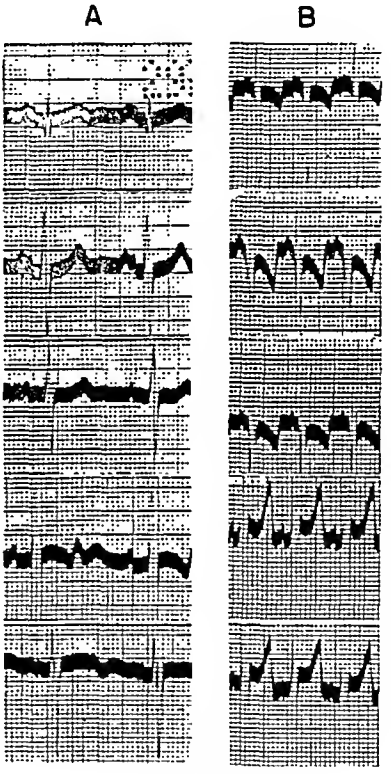

FIG. 4.

FIG. 3.—Three different patterns of combined ventricular strain. (A) shows the "concordant type of left ventricular preponderance" (Type III pattern of combined ventricular strain) in a 35 year old patient with hypertension and chronic emphysema. Heart weight at autopsy was 830 g., all chambers being dilated and hypertrophied. Note S–T depression and T inversion in all the limb leads as well as absence of axis deviation. (B) shows the "concordant inverted type of heart strain" (Type IV pattern of combined ventricular strain) in an 11 year old patient with mitral stenosis and insufficiency. QRS is of the S type in all leads. Note the large P waves in leads I and II. (C) shows prominent S waves in all three limb leads without inversion of QRS (Type V pattern of combined ventricular strain) in a 54 year old patient with stenosis and insufficiency of the mitral and aortic valves, hypertension, and emphysema and auricular fibrillation.

FIG. 4.—(A) shows the Type VI pattern of combined ventricular strain diagnosed on the basis of a small upright QRS in lead I and diphasic QRS complexes in leads II and III with deep S waves. The record was taken on a patient of 25 with mitral and aortic stenosis and insufficiency. Note the normal QRS contour in the chest leads and the typical "mitral" P wave pattern in limb and chest leads. (B) was taken on a three month old infant with Von Gierke's disease and marked cardiac enlargement, proven at autopsy. Combined ventricular strain was diagnosed because of the S–T depressions and T inversions in all limb leads. Note the large diphasic QRS complex in lead I.

In our 11 cases of this Type III pattern (Fig. 3 A), 8 were accounted for on the basis of combined heart strain; 3 of these were in cases of hypertension and chronic cor pulmonale due to asthma, bronchiectasis, and emphysema; 3 were due to combined mitral and aortic valvular lesions; 1 was due to hypertension combined with mitral stenosis; and the last was a case of severe hypertension with pulmonic valvular incompetence, either organic or functional. Of the 3 remaining cases, one had only hypertension, although X-ray showed enlargement both to the right and left, another had hypertension with only left-sided enlargement, and the third had only left ventricular hypertrophy with displacement of the heart and mediastinum to the right by massive pleural effusion from a pleural fibrosarcoma (reported with autopsy by Kaplan and Katz, 1941). Two of the cases, one with hypertension and emphysema and one with combined valvular disease, also came to autopsy, the hearts weighing 675, 725, and 830 g. respectively and showing bilateral ventricular hypertrophy.

None of the 7 cases with concordant inversion of the QRS in the limb leads showed large Q waves (Type IV). In the only case coming to autopsy, bilateral ventricular enlargement was present in association with an inter-atrial septal defect, the ætiology of the left ventricular enlargement not being evident. In all of the remaining 6 there was clinical evidence of bilateral strain. One of these appeared to be due to a combination of severe hypertension and chronic emphysema on an asthmatic basis, while a second (Fig. 3 B) had rheumatic mitral stenosis and insufficiency to account for the combined strain, although X-ray showed only slight cardiac enlargement. In the remaining 4 cases, congenital heart disease was present, 2 of these having an associated rheumatic mitral stenosis and regurgitation. The relative frequency of congenital heart disease in this type is striking, and one must consider the possibility that the abnormally directed QRS complexes may represent a congenitally abnormal pathway for the spread of the impulse rather than evidence of bilateral ventricular strain, although the latter is often present in congenital heart disease. This Type IV pattern is present in many of Schnitker's (1940) autopsy series of 106 cases of congenital cardiac disease.

There were 3 cases of the Type V pattern. These are similar to the preceding patterns in that S waves are present in all the limb leads, but differ in that the major deflection is not directed downward in all the limb leads. One of these came to autopsy and showed bilateral ventricular hypertrophy due to mitral and aortic lesions and in addition a patent foramen ovale. In the other two, X-ray showed cardiac enlargement both to the right and left. Both of these had mitral and aortic lesions with stenosis and regurgitation; one of them also had hypertension and emphysema (Fig. 3 C). The criteria for the differentiation of records such as these from those instances of normally occurring S waves in all the limb leads have already been discussed (39).

There were 18 instances of the Type VI pattern. Clinical or autopsy evidence of combined ventricular strain was present in two-thirds of these, autopsies of 7 being available. Of the 12 cases with combined strain, 3 had emphysema and hypertension, 3 had mitral stenosis and insufficiency, 2 had deformities of both mitral and aortic valves (Fig. 4 A), 1 showed severe coronary sclerosis and myocardial fibrosis with bilateral ventricular hypertrophy (heart weight 500 g. at autopsy), 1 showed bilateral hypertrophy (heart weight 475 g. at autopsy) with no demonstrable cause, and 2 showed bilateral hypertrophy with emphysema to explain that of the right ventricle, while the cause of the left ventricular hypertrophy was not disclosed. In the remaining 6 of this type none showed evidence, either clinically or anatomically, of combined ventricular hypertrophy, and only one showed any cardiac enlargement at all, this being in an autopsied case of emphysema with marked right ventricular enlargement. In two other cases, pulmonary emphysema was present with a resultant vertically placed heart which was not enlarged; another autopsied case showed brown atrophy of the myocardium with no other abnormalities; and in the last two cases of this group, one of which came to autopsy, there were no abnormal cardiac findings although the position of the heart was not recorded.

The frequency of pulmonary emphysema in cases showing this cardiographic pattern was striking, being present in 8 of the 18 cases (45 per cent). In these cases there was a vertically placed heart and a rotation of the heart on its longitudinal axis from right to left due to the low position of the diaphragm. It has been shown (18, 35) that this position change may be the sole abnormality in cases having this cardiographic contour, and this may be the mechanism in 3 of our cases with normal-sized hearts. Since emphysema also was present in 5 of the cases that had bilateral ventricular strain, it is possible that cardiac displacement played the major role in determining the abnormal QRS contours. However, the fact that this pattern occurred in 7 cases of bilateral enlargement without emphysema indicates that combined strain does give rise to this pattern *per se*.

The last record (Fig. 4 B) which did not fit any of the above patterns was taken from a three month old infant with Von Gierke's disease (confirmed by autopsy) in whom the heart was massively enlarged. The diagnosis of combined strain was based primarily on the depression of the S–T segments and deep inversion of the T waves in all the limb leads associated with a large equiphasic QRS_1 with deep S_1.

In order to estimate the frequency of the cardiographic patterns suggestive of combined ventricular

strain which occur in combined ventricular hypertrophy, a series of 149 consecutive autopsies in which cardiograms were available (Katz *et al*, 21) were reviewed. After eliminating cases with myocardial infarction, acute cor pulmonale on the basis of massive pulmonary embolism, and intraventricular block (QRS duration of 0·12 sec. or more) in the cardiogram, 29 cases remained in which the hearts were enlarged and both ventricles hypertrophied. The distribution of the patterns is shown in Table II. In over 25 per cent. of the cases with bilateral ventricular hypertrophy evidence

TABLE II

CARDIOGRAPHIC CONTOURS IN 29 AUTOPSIED CASES OF BILATERAL VENTRICULAR HYPERTROPHY

Cardiographic Pattern	No. of Cases	Percentage of Series
No axis shift or normal right or left axis shift	10	35
Left ventricular preponderance	8	27·5
Right ventricular preponderance	3	10
Combined ventricular strain	8*	27·5

* The eight records showing evidence of combined ventricular strain fell into the following types (see Table I): 2 into Type I, 2 into Type III, 1 into Type IV, 1 into Type V, and 2 into Type VI.

of this was visible in the cardiogram. It is thus apparent that the occurrence of these particular patterns should suggest the possibility of combined ventricular strain, when myocardial infarction, acute cor pulmonale, and digitalis effect have been ruled out, provided, of course, that the QRS duration is normal. Obviously, when there is clinical and radiological evidence of cardiac enlargement and the cardiogram shows no evidence of preponderance or only a normal right or left axis shift (as in 35 per cent of our autopsied series (Table II)), bilateral ventricular strain may still be present, the assumption being that the pattern of strain on one ventricle neutralizes that of the other almost completely. Furthermore, while these patterns are suggestive of combined ventricular strain, and in the cardiographic series analysed were substantiated clinically or by autopsy in 81 per cent of the cases, it does not follow that the pattern is directly due to the hypertrophy of both ventricles. In some instances the displacement of the heart and its rotation on its various axes may contribute to these so-called combined strain patterns. Furthermore, in some instances, it is not at all impossible that disseminated focal lesions may sufficiently alter the spread of the impulse to give rise to these patterns without accompanying prolongation of the total invasion time. This may also be brought about in congenital heart disease, by a congenitally abnormal placement of the conduction system. Until such a time as more definite evidence is available, the exact mechanism leading to these patterns must be considered *sub judice*. This, however, does not nullify the diagnostic significance of such records.

SUMMARY AND CONCLUSIONS

An analysis of 47 cases showing a combination of features of right and left ventricular strain in the cardiogram is presented. These were then correlated with clinical data and, in 19 instances, with the available autopsy findings.

Six electrocardiographic patterns of combined ventricular strain are described.

The cardiographic diagnosis of combined ventricular strain was substantiated by clinical, radiological, or post-mortem evidence in 81 per cent of the cases.

In a control group of 29 autopsied cases of bilateral ventricular hypertrophy in the absence of myocardial infarction, acute cor pulmonale, intra-ventricular block, or digitalis effect in the cardiogram, cardiographic evidence of combined strain was present in 27·5 per cent. In 35 per cent of the same series no ventricular preponderance and no axis deviation or only normal right or left axis shift were present; this substantiates the statement that absence of ventricular preponderance in the cardiogram in the presence of clinical or radiological evidence of cardiac enlargement is presumptive evidence of combined ventricular strain.

Other factors like displacement of the heart, congenital anomaly of the conduction system, or focal intraventricular block may be responsible for a pattern suggestive of combined ventricular strain.

Further anatomical correlation studies are necessary to establish the diagnostic accuracy of the cardiographic patterns of combined ventricular strain.

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Addendum

While this article was in press, Schwartz and Marcus (Schwartz, S. P., and Marcus, H. (1942) *Amer. Rev. Tuberc.*, 46, 35) reported a number of cases of our Type IV and several of our Type VI pattern. These patterns occurred predominantly in cases of chronic cor pulmonale. From their autopsy data in 7 such cases, as well as in 2 additional cases of congenital heart disease, the patterns appear to be most commonly associated with predominant hypertrophy of the right ventricle. However, they also occurred in the absence of ventricular hypertrophy when the right ventricle was dilated.

PAROXYSMAL VENTRICULAR TACHYCARDIA

BY

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Paroxysmal ventricular tachycardia is comparatively rare. It was first differentiated from paroxysmal auricular tachycardia by MacKenzie (1908) through his study of simultaneous venous and arterial tracings. Others (Franck, 1894, and Hoffman, 1900) had hinted that this might be the case. The following year Lewis (1909) published the first electrocardiogram that supported this contention; the rhythm consisted of numerous isolated or continuous extrasystoles, eleven being the most occurring in one run.

Since Lewis's pioneer studies (1909, 1910), many workers have brought about a clearer conception of the condition and its prognostic significance. Their articles will be considered in more detail elsewhere in this paper.

DIAGNOSIS

Clinical evidence. Levine and Strong (1923) pointed out that it may be possible to make a diagnosis of ventricular tachycardia at the bedside. In auricular tachycardia the rhythm on auscultation appears to be absolutely regular. In ventricular tachycardia, however, there is sometimes an arrhythmia and sometimes a variation in the intensity of the first heart sound. Whether, however, it is possible to differentiate with any certainty this condition when showing arrhythmia from paroxysmal flutter with varying block or even from fibrillation at the rate of about 140, is extremely doubtful. Gallavardin (1920) and Prinzmetal and Kellog (1934) again drew attention to MacKenzie's observation that the presence of ventricular tachycardia can be shown by observation of the jugular pulse; regularly recurring auricular waves at a slower rate than the pulse rate may be noted in some cases.

There is one further point that could be of some assistance in the diagnosis: the occurrence of a sudden marked rise and fall in the pulse rate in a patient with long-standing auricular fibrillation means that the episode is probably due to paroxysmal ventricular tachycardia, especially after heavy digitalization. Any of these points might suggest the diagnosis but the final and only proof is the electrocardiogram.

Electrocardiographic records. Robinson and Herrman (1921) were the first to lay down the diagnostic criteria—"The electrocardiogram must show that the cardiac impulses are arising in the ventricles and this is most clearly shown when a succession of auricular complexes can be made out occurring independently of and at a slower rate than the complexes of ventricular origin. The ventricular complexes are distinctly abnormal in form. This alone, however, cannot be taken as absolute proof as changes in form may be caused by changes in intraventricular conduction. When records made between attacks show there is no such disturbance then, the ventricular origin of the tachycardia is very probable, although disturbances of conduction may appear at a high cardiac rate which are not apparent when the heart is beating slowly. The presence of isolated ectopic beats before or after a paroxysm is evidence in favour of the tachycardia being ventricular, especially when the form of the complexes of the isolated beats is the same as the form of those of the paroxysm."

The presence of ectopic beats, however, before or after a paroxysm has no diagnostic significance, though Campbell and Elliott (1939) believe that where supraventricular extrasystoles are observed, the paroxysms are always of auricular origin. Amongst the cases to be described here, there are some with auricular premature beats occurring before and after the paroxysms of ventricular origin (Fig. 1). Isolated complexes identical with those of the paroxysm are almost impossible to find: the criteria should be changed so that the complex of an ectopic ventricular beat which is almost the same as those of a tachycardia may denote the ventricular origin of the paroxysm (Fig. 2 and 18).

* This work was done while holding a Research Fellowship in Medicine, Harvard University, 1938–39, and Walter Myers Travelling Studentship, Birmingham University, 1938–39. The basis of this paper formed part of a thesis submitted by one of us (W. T. C.) and accepted for the degree of M.D. of the University of Cambridge.

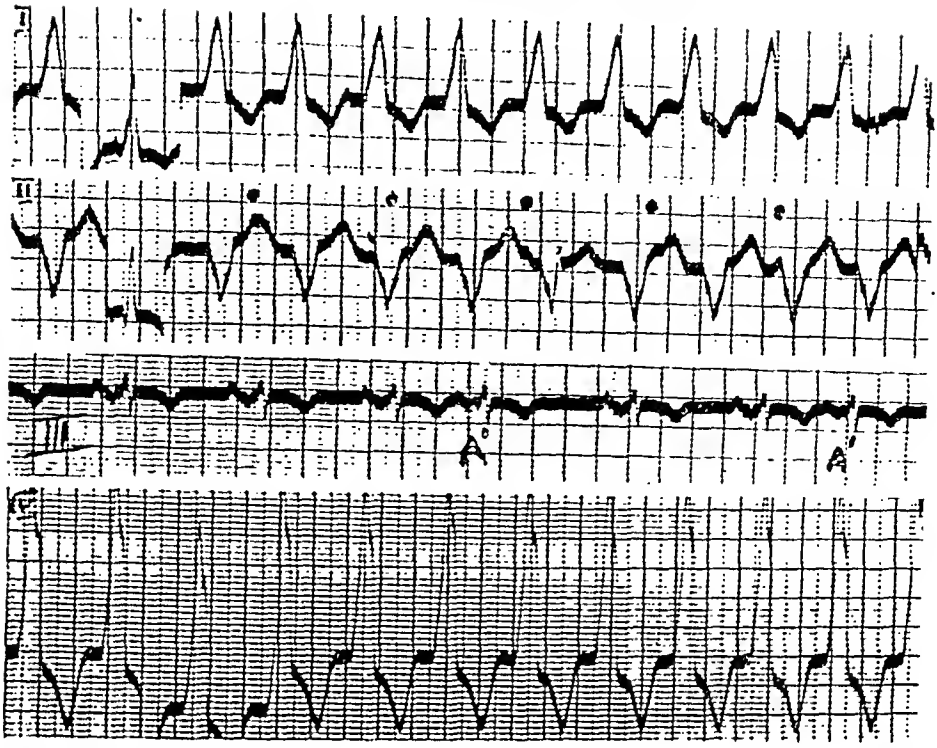


FIG. 1.—Case 22. Ventricular paroxysmal tachycardia, rate 140; auricular rate 75. Breaks in the ventricular rhythm in leads I and II are shown. The single beat in lead I simulates the Wolff-Parkinson-White type. Two premature auricular beats are shown during normal rhythm in lead III (marked A). The dots indicate the site of P waves.

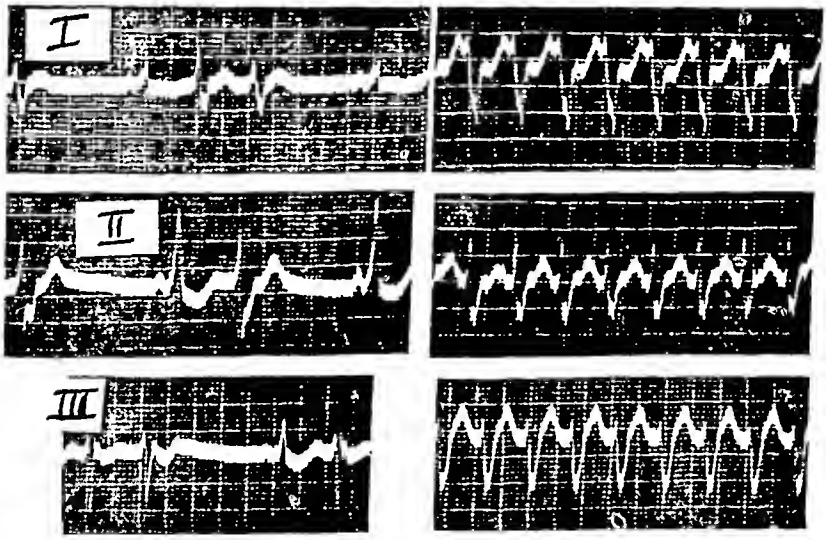


FIG. 2.—Case 27. Wolff-Parkinson-White type. On the left, S-A rhythm with numerous ventricular extrasystoles. On the right, paroxysmal ventricular tachycardia. No P waves can be identified but the ventricular complexes are sufficiently similar to the extrasystoles during normal rhythm to make the diagnosis.

Further, as has been suggested above, a succession of abnormal ventricular complexes occurring regularly and at a rate faster than the usual ventricular rate in the course of auricular fibrillation denotes ventricular tachycardia.

Lewis (1925) pointed out that it is difficult to be certain of the origin of paroxysmal tachycardia in any given example unless P waves or the beginning or end of the paroxysm are recorded. The actual mode of ending is not always a reliable index, as the compensatory pauses and the normal rhythm after both auricular and ventricular tachycardias is subject to great variation. However, on a few occasions the T wave of the last complex of a paroxysm is not the same as the remainder, thus providing evidence of superimposed and hidden P waves on the remaining T waves and so of its auricular origin. But in many examples of known auricular tachycardia this may be difficult to detect.

Strong and Levine (1923) carefully measured the time intervals between the QRS complexes and pointed out that there was much variation as opposed to the comparative regularity of auricular paroxysmal tachycardia. This has been used by some in differentiating the doubtful cases. We have, however, encountered cases of very regular rhythm in ventricular, and of considerable arrhythmia in auricular tachycardia. Too much stress has been laid on the irregularity.

Radiology. Kahlstorf (1936) states that with the kymograph it is possible to present indisputable evidence. He recorded one case of paroxysmal auricular tachycardia in which he was able to demonstrate the auricular rate of 280 satisfactorily by this method. He suggested that the method should be tried in ventricular tachycardia, and it might perhaps be useful where the diagnosis is doubtful.

Differential diagnosis. Some of the difficulties in diagnosis have already been mentioned. They can be well illustrated by Fig. 3, which was originally interpreted as showing ventricular tachycardia. It is, however, impossible to make out any auricular activity and the shape of the ventricular complexes may be due to aberration, so that one would not be justified in a definite diagnosis. The influence of the rate can well be shown in Fig. 4. The first record shows auricular flutter (A, 270; V, 135), while the second, taken in another attack with the same auricular rate, showed a 1 : 1 response of the ventricles but with aberration of the ventricular complexes.

Cases of the type described by Wolff, Parkinson, and White with a short P–R interval and wide QRS complexes cause some difficulty in diagnosis. They frequently maintain their abnormal complexes during a paroxysm or they may develop a greater degree of aberration or indeed actual ventricular tachycardia which is, however, rare (Fig. 2). Only a few other cases of ventricular tachycardia complicating this syndrome have been reported (Levine and Beeson, 1941). One of us (P. D. W.) believes that another case (Fig. 5) also shows paroxysmal ventricular tachycardia but it is not possible to identify any regular P waves or satisfy the other criteria laid down, so that paroxysmal auricular fibrillation cannot be ruled out as a possible diagnosis. Such rhythms in this type have caused difficulties in diagnosis on many occasions (Fig. 6).

These difficulties in diagnosis amply illustrate the necessity of applying strict criteria to the interpretation of the electrocardiograms in these cases.

Criteria for diagnosis. In the cases that are reported here, the following four electrocardiographic criteria have been applied.

1. The presence of P waves at a slower rate than that of the ventricles, during a paroxysm of tachycardia (Fig. 1).
2. A paroxysm of abnormal ventricular complexes, i.e. three or more at a rapid rate, occurring during auricular fibrillation (Fig. 7).
3. The onset of the tachycardia with an abnormal ventricular complex (Fig. 8).
4. Close resemblance of the complexes of ventricular premature beats to the complexes occurring during paroxysmal tachycardia (Fig. 2 and 18).

Any one of these conditions establishes the diagnosis of paroxysmal ventricular tachycardia.

Present Study

Number of cases. All cases of ventricular paroxysmal tachycardia occurring in the cardiographic records of the Massachusetts General Hospital during the 25 years from 1914 to 1939 have been collected. These were 24 cases among 51,000 records from about 25,000 patients. There were in addition, 3 patients whose tracings had been taken elsewhere. Three patients have previously been reported (Case 24, Jones & White, 1926; and Cases 1 & 9, Palmer & White, 1928). In addition to these 27 cases, there have been included in the appendix 5 further cases that had been diagnosed previously as ventricular but should be classed as doubtful or auricular in origin.

Ætiology. Of the 27 cases, 22 had coronary heart disease; 4 of these were still living when this study was completed in 1939, and 1 had not been traced. The remaining 5 had no other cardiac abnormality; 4 were alive and 1 had not been traced.

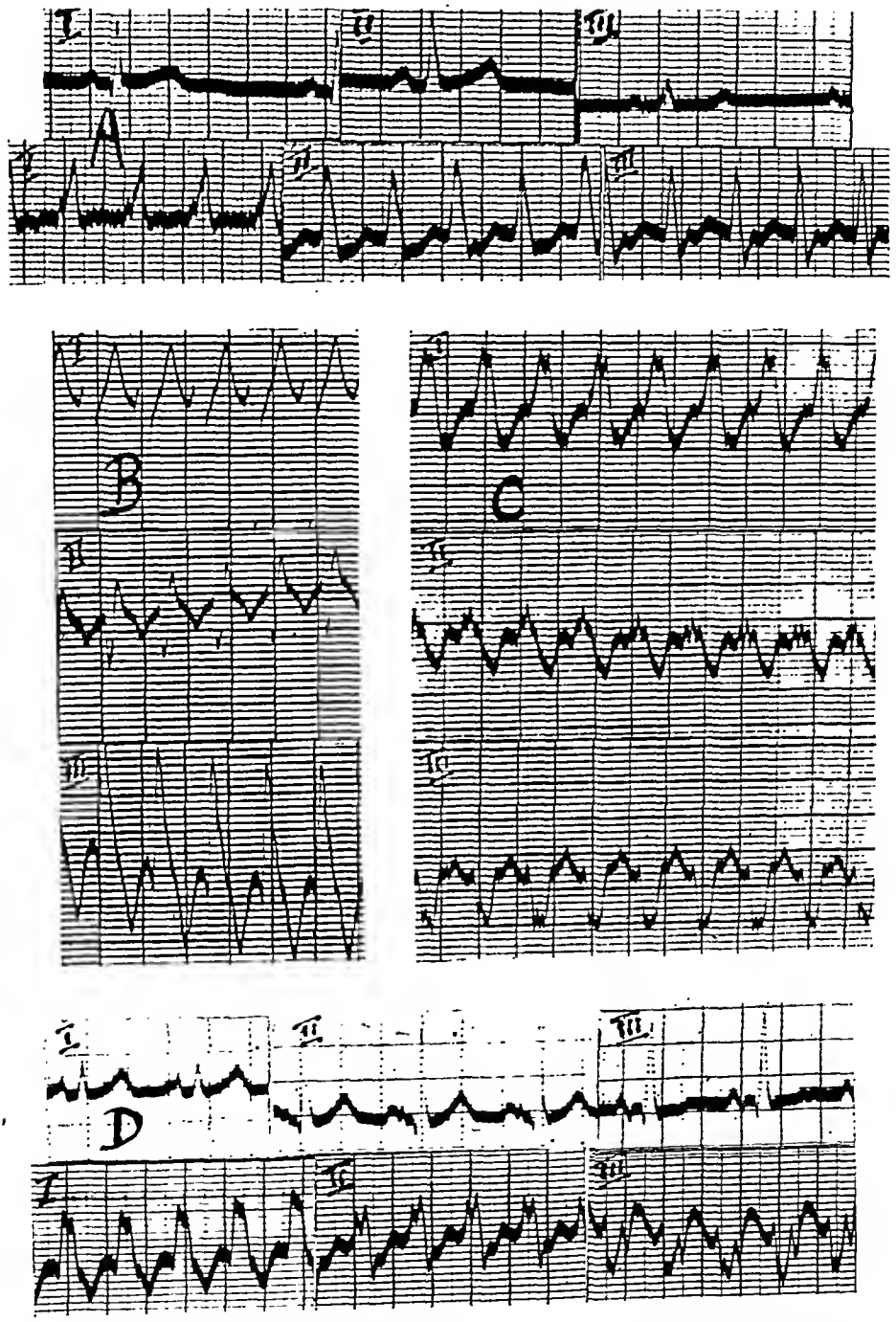
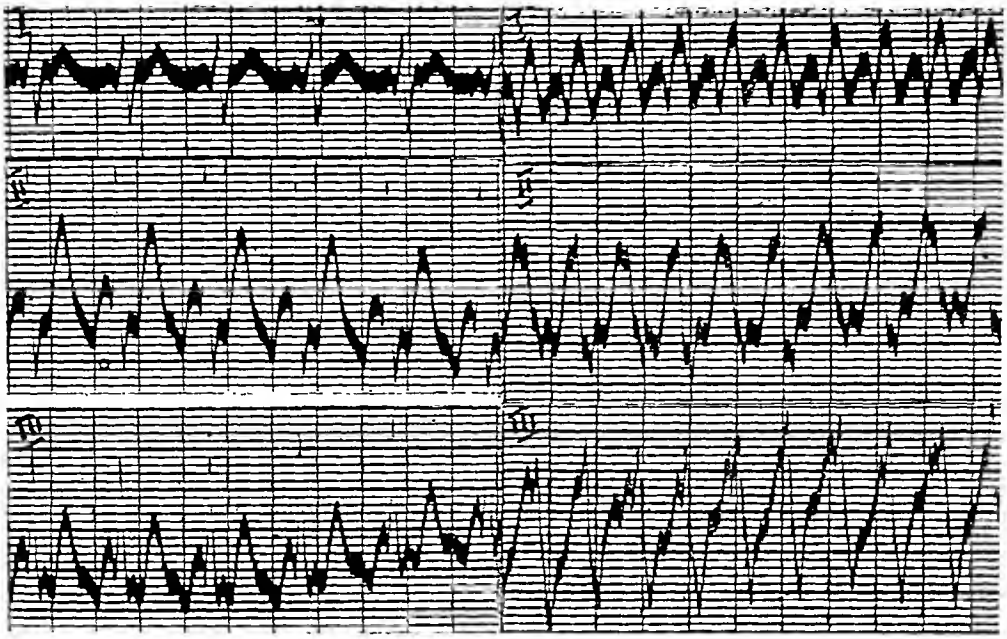
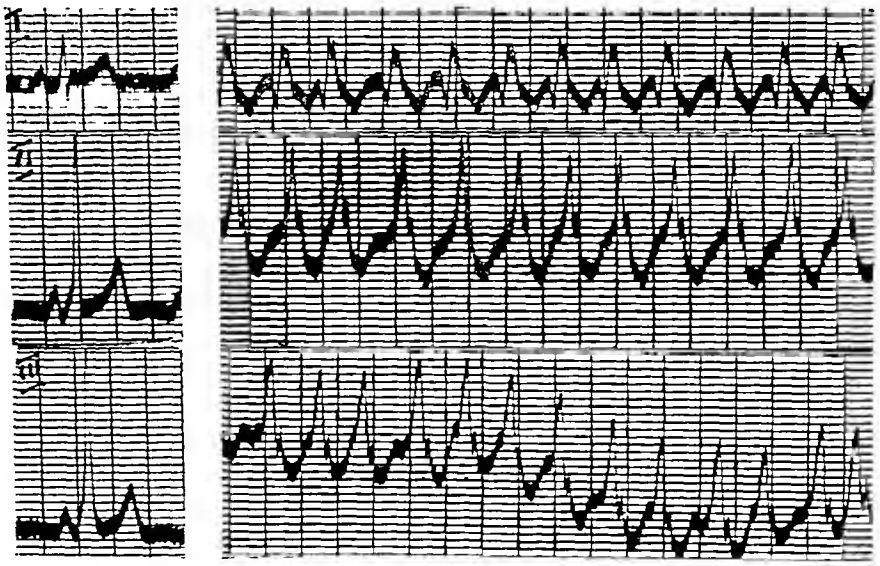


FIG. 3.—Short tracings from four patients (see appendix) in which there was insufficient evidence to make a diagnosis of paroxysmal ventricular tachycardia.
(A) and (B) are probably auricular in origin with aberrant conduction in the ventricles due to the rate, while (C) and (D) are possibly ventricular. No definite P waves can be made out in any of the records.
(A) Case 28. (B) Case 29. (C) Case 30. (D) Case 32.



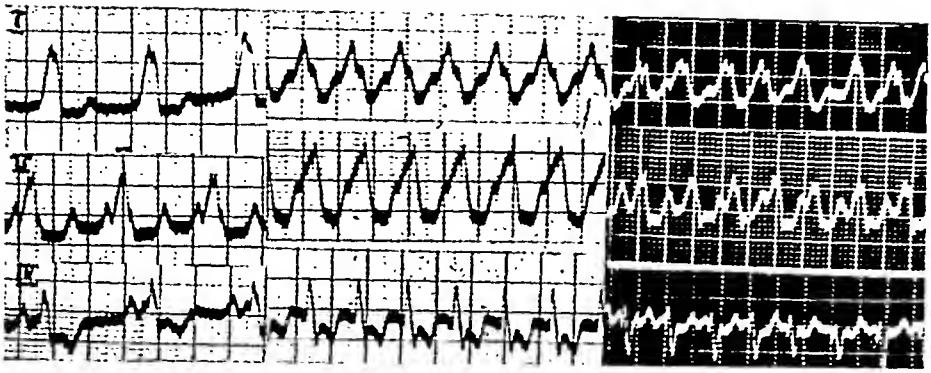
A B

FIG. 4.—Electrocardiograms, one of which simulates ventricular paroxysmal tachycardia. Both are from the same patient, and the auricular rate in each is 270, but 2 : 1 block is present in (A) and in (B) there is an aberrant ventricular response to every auricular beat.



A B

FIG. 5.—Case 31. On the left (A), normal rhythm with a short P–R interval and wide QRS complex (Wolff-Parkinson-White type). On the right (B), either paroxysmal ventricular tachycardia or paroxysmal auricular fibrillation. Possible P waves can be made out but no regular rhythm can be shown. The diagnosis must remain doubtful.



A B C

FIG. 6.—Wolff-Parkinson-White type. (A) Normal rhythm, (B) paroxysmal auricular tachycardia (or flutter), and (C) paroxysmal auricular fibrillation. All three records from the same patient, illustrating similarities in appearance to ventricular tachycardia.

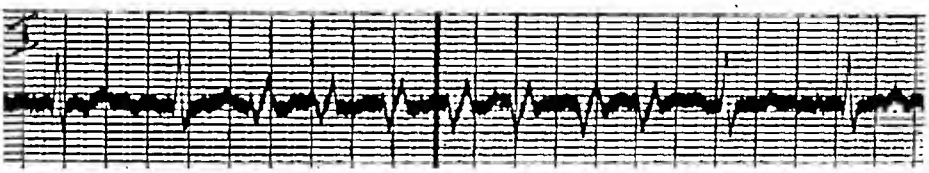


FIG. 7.—Case 17. Short paroxysm of ventricular tachycardia occurring during auricular fibrillation.

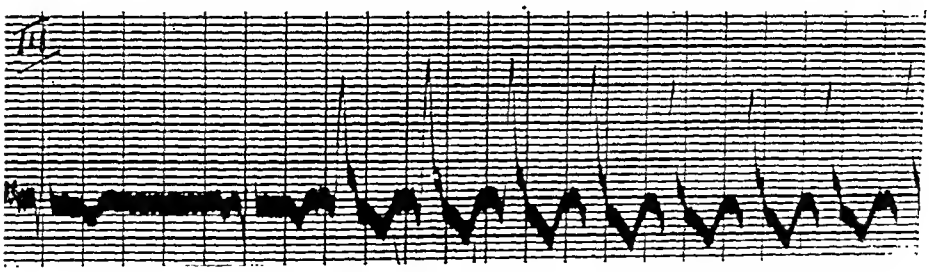


FIG. 8.—Case 24. Onset of a paroxysm shortly after the end of a T wave.

Sex incidence. 17 were males and 10 females. This ratio is somewhat higher for females than the figures that were given by Lundy and McLellan (1934) who found in their analysis of 94 reported cases that there were 68 males and 26 females: 14 of these 94 cases had no other cardiac abnormality.

Age incidence. The age incidence of our group is shown in Fig. 9. The table given by Strauss (1930) has been used for comparison (the lower part of the columns) and the figures of our group have been added (in the upper part of the columns). As would be expected, the greatest incidence accompanies the decade with the greatest incidence of coronary heart disease.

The youngest patients recorded have been aged 13 (Beeson & Levine, 1941), and 16 (McMillan & Bellet, 1932, and Lundy & McClellan, 1934). Our youngest patient (Case 24) was aged 18), but his father, a physician, had observed the attacks since the age of five.

THE ROLE PLAYED BY DIGITALIS

Traube (1851) pointed out that large doses of digitalis at first slow the heart and later increase the rate to one far exceeding that of the normal heart. This he supposed was due to the paralysis of the vagus.

Francois-Franck (1894), as a result of his experiments, described in remarkable detail the various disturbances of rhythm that took place. The digitalis arrhythmia was characterized by: repeated

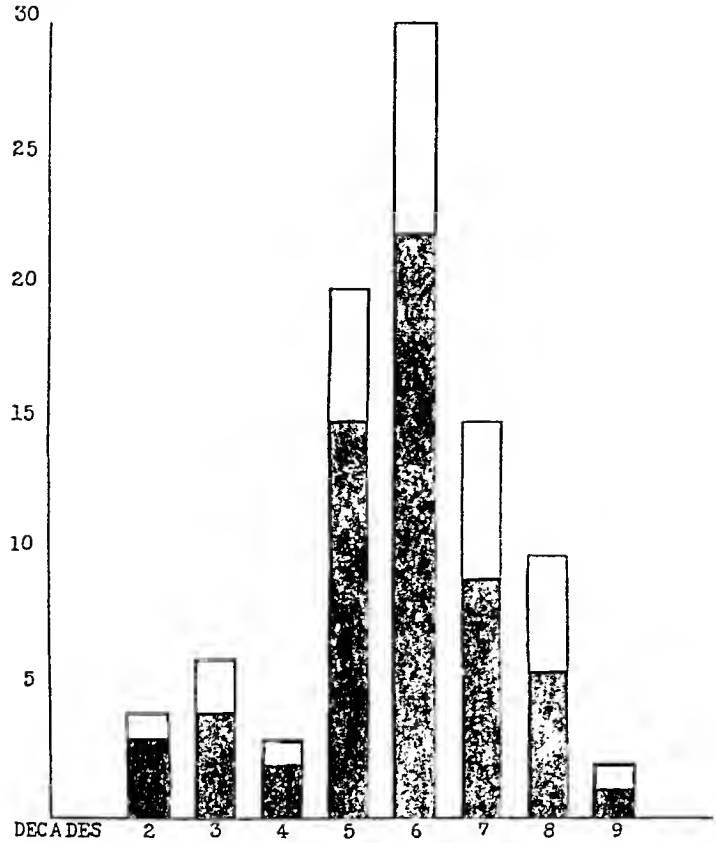


FIG. 9.—The age incidence of paroxysmal ventricular tachycardia. The figures for this series have been placed above those given by Strauss (1930), making a total of 90 cases in all.

close beats in groups of two, three, or more, producing the bigeminal or trigeminal pulse; numerous extrasystoles that are scarcely perceived at the wrist; groups of semi-tetanic contractions; intermittence of the heart for varying periods; and regular beats, with or without extrasystoles, between two periods of tachycardia. He completed his description—" Tous les désaccordes sont possible sous l'influence de la digitaline entre la fréquence et le rythme auriculaires et la fréquance et le rythme ventriculaires: les modifications des ventricules ne sauraient dône être subordonnées à celles de l'oreillette."

Cushny (1897), in his very extensive researches, noted exactly the same phenomena and believed that they were due to the increasing irritability of the cardiac muscle. All these findings were later confirmed by Robinson and Wilson with the aid of the electrocardiograph (1918).

Turning from experimental to clinical evidence, Vaughan (1918) suggested that the tachycardia observed in his two cases might be due to digitalis. Schwensen (1922) reported two cases and wrote that probably the administration of digitalis directly caused the attacks of ventricular tachycardia. He suggested that the sudden and unexpected deaths of patients under digitalis therapy was due to ventricular fibrillation resulting from overdosage.

Danielopolu in the same year (1922) published a report of three cases which he had observed in 1911 and 1913 and also ascribed them to digitalis or strophanthus. From the records published (pulse tracings) it is difficult to be sure of the exact nature of the tachycardia.

During the next few years there were numerous reports which illustrated the potentialities of digitalis in producing this rhythm (Fellerbaum, 1923; Reid, 1924; Marvin, 1928; etc.). Luten (1924, 1925) showed quite convincingly in a series of articles, the similarity between over-digitalization in animals, as demonstrated by Robinson and Wilson, and in patients. He regarded the alternation of the ventricular complexes which was being noted fairly frequently in such cases as the stage of intoxication just prior to fibrillation, and as an effect upon the conduction system rather than upon the muscle.

Gilchrist in 1926 recorded 5 cases of ventricular paroxysmal tachycardia and showed conclusively in one case that the abnormal rhythm appeared only upon the administration of digatalis and disappeared when the drug was withdrawn. Strauss (1930) found that of the 64 cases recorded

to that time, digitalis had been administered before the onset of the tachycardia in about 50 per cent, and of these there were some excessive doses while in others the dose was probably too small to have any effect. However, as Gilchrist had pointed out, and as Scherf and Kisch pointed out later, in very damaged and abnormal hearts even small doses of digitalis may be sufficient to cause abnormalities of rhythm.

An excellent commentary and summary of the effects of digitalis is given by Scherf and Kisch (1939), who reported the results of their observations, extending over fourteen years, upon 18 patients with ventricular paroxysmal tachycardia and alternating complexes. In 14, digitalis was probably the provoking and determining factor, but in 4 no digitalis was given; in these latter cases, they believed that there was gross myocardial damage. They thought that digitalis cannot produce the arrhythmia unless the heart is already damaged, because Kobacher and Scherf (1930) were unable to produce such arrhythmias in normal hearts of animals, and also because the reports of cases of suicide contain no mention of the production of any arrhythmia (e.g. Albeaux, Fernet, & Welti, 1939). In some of their cases the tachycardia frequently disappeared if the digitalis was discontinued but it returned if the drug was given again. On the other hand, tachycardia may not develop after the administration of excessive amounts of digitalis over a long period. They, therefore, assumed that the quantity of digitalis administered is not the factor of exclusive importance, but that the state of the heart muscle is chiefly responsible. They recorded one case in which the rhythm disappeared only during the administration of large doses of quinidine and of digitalis, in a young man aged 23 years.

There were 12 out of our 27 cases to which no digitalis had been given before the onset of the tachycardia. Of these, 5 were cases in which the only apparent abnormality was the arrhythmia, i.e. with presumably normal hearts. Of the 15 cases to which digitalis had been given, there were 5 in which the dosage had been greater than normal, and we are warranted in assuming that digitalis played a large part in the production of the paroxysm (Cases 2, 5, 6, 13, & 18; see appendix). There were 10 other cases to which digitalis had been given prior to the tachycardia (Cases 1, 3, 4, 8, 9, 10, 11, 16, 17, & 19).

Of the 7 cases of coronary heart disease that had had no digitalis before the onset of the tachycardia, there were 4 to which digitalis was administered in average doses after the onset (Cases 14, 20, 21, & 22).

There remain 5 cases of apparently normal hearts with ventricular paroxysmal tachycardia. These all had digitalis given to them at one time or another, in various dosage, without any noticeable effect, either in increasing the frequency or diminishing the number of the attacks.

To summarize, out of 22 cases of coronary heart disease showing ventricular paroxysmal tachycardia, 5 were probably related to digitalis administered, and 3 others may possibly have been so related; 1 in which no digitalis had been given before, may have been aggravated by digitalis; 7 had had digitalis but probably in doses that were unrelated to the tachycardia; 3 had had digitalis after the tachycardia without any aggravation of symptoms; and the remaining 3 had no digitalis at any time.

There had been no case in this series in which the ætiological role of digitalis was proved by therapeutic test, but it was probable in some of the cases. It is very likely, as Scherf and Kisch point out, that the quantity of digitalis is not the primary factor but rather the state of the heart muscle. One may go further and suggest that it is the state of the conducting tissues rather than of the contractile tissues that is of major importance.

Some cases of ventricular tachycardia could have been prevented. The method of rapid digitalization was popularized in 1920 and the danger involved has been generally realized only in recent years. The occasions for excessively rapid digitalization are not very common. Digitalis folia takes six hours before it begins to exert its maximum effect and yet it is extremely common to find the drug prescribed at three or four hourly intervals, thus allowing overdosage before the appearance of toxic symptoms. Six hourly intervals would be more rational.

Digitalis intoxication may arise, moreover, in a previously digitalized patient with the onset of diuresis and the liberation of large amounts of the digitalis that had been stored in the tissue fluids. It is quite possible to incriminate this mechanism in our cases. On looking through the reported cases and our own, the plea for more care in the use of digitalis seems wholly justified.

Rate and Rhythm of the Paroxysms

There is a great variation in the rate of the individual paroxysms. In this series the slowest is about 100, while the most rapid is 270. The average speed for 30 different paroxysms occurring in these 27 cases is 174. Campbell and Elliott (1939) found an average rate of 198 in their eight ventricular cases. There is no definite correlation to be found between the rate and the prognosis, although it is true that of the three patients with rates below 140, two died within a few hours while the third

was alive two years after the episode, and that the extremely fast rates of 250 and 270 were found in patients with otherwise normal hearts.

It is not uncommon for both auricular and ventricular paroxysmal tachycardia to show some irregularity in the timing of the complexes in the first two or three beats before taking on the regular rhythm of the paroxysm. Three cases of this group illustrate a gradual change in rate, either speeding up or slowing down of the rate of the paroxysm. Case 18 (Fig. 10) showed a gradual increase in rate,

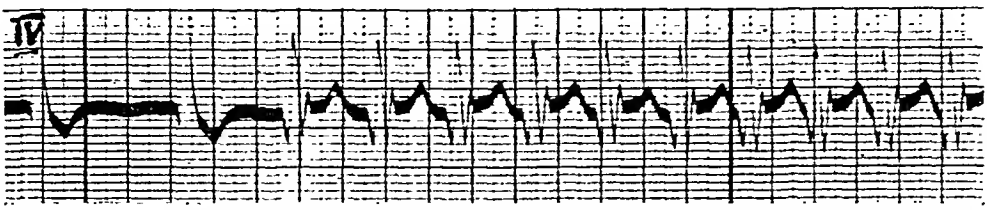


FIG. 10.—Case 18. Onset of paroxysmal ventricular tachycardia with abnormal ventricular complexes. There is a gradual increase in rate from 150 to 190 beats per min. Lead IV (old technique).

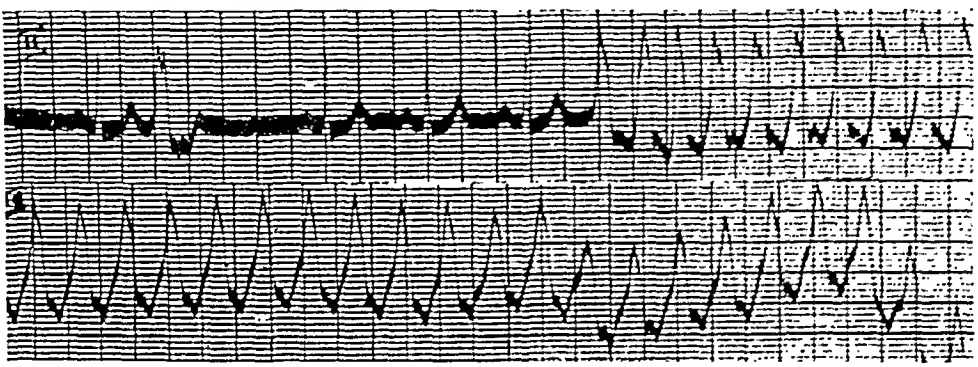


FIG. 11.—Case 26. Onset of paroxysmal ventricular tachycardia at a rate of 270 and gradual decrease to 220 beats a minute.

over about six beats from 150 until the rhythm appears to become regular at 190. Case 24 also showed a slight tendency to speed up. Case 26 (Fig. 11) showed the opposite phenomenon, starting at 270 and slowing down over the space of many seconds to the rate of 220.

Levine and Strong (1923) reported that while the intervals were regular in paroxysmal auricular tachycardia, they showed slight irregularity in ventricular tachycardia. They reported and gave illustrations of three cases. Probably, however, their Case 3 was not ventricular tachycardia but auricular flutter with aberrant ventricular response, the auricles beating at a rate of 280–300 and the ventricules responding with 4 : 3 block and some slight regular variation in A-V conduction. This would explain the great regularity in the irregularity of the intervals. The second case also may not be ventricular paroxysmal tachycardia for it is unusual to find both auricular and ventricular paroxysms in the same patient and the records that are given of the two conditions are not from the same lead. In the example of ventricular tachycardia given, the onset of the paroxysm is shown, but it is impossible to be certain that there is no P wave hidden in the preceding T wave or to identify any P waves in the ensuing paroxysm. Partly as a result of this article, there has arisen an exaggerated impression as to the irregularity of ventricular tachycardia. Irregularity of the nature or of the extreme degree shown in Levine and Strong's third case is extremely uncommon and should always lead to a search for some other mechanism.

Irregularity that can easily be seen on the tracings, is usually present in cases arising during auricular fibrillation (our Cases 8, 10, 17, & 20). It is present in an occasional case when the patient is very nearly dead (Case 12). Some irregularity is usually present in very short paroxysms, as in our own Case 23 where the measurements are shown on the electrocardiogram (Fig. 12). Among 15 of the tracings, however, in which there is a definite and prolonged paroxysm, 13 are perfectly regular, 10 as measured by calipers and time interval lines (Cases 3, 4, 5, 6, 14, 15, 19, 24, 25, & 27) and the other 3 (Cases 1, 11, & 22) as measured by the Lucas comparator. Case 13 appears to be irregular and the measurements of Case 2 show some slight irregularity. McKinnon (1934) also has found that the rhythm of the great majority of cases of paroxysmal ventricular tachycardia is perfectly regular.

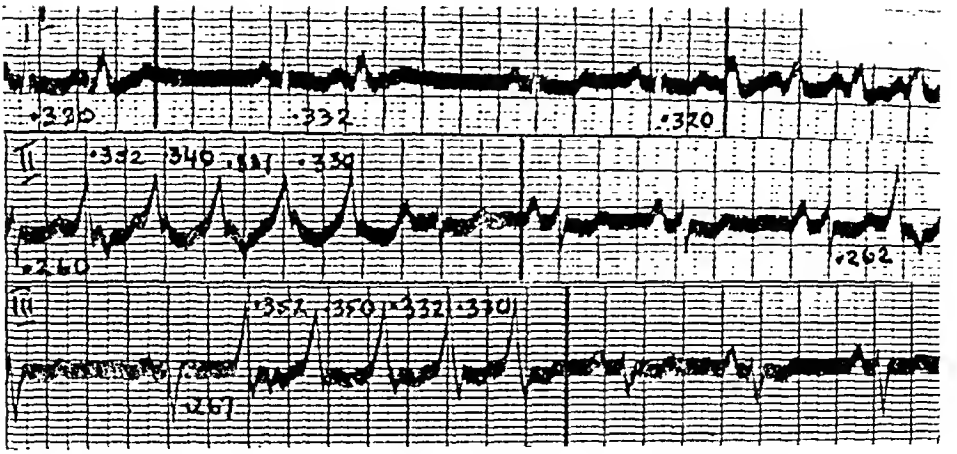


FIG. 12.—Case 23. Numerous short paroxysms of ventricular tachycardia. Comparator measurements show slight irregularity during the paroxysms. The onset of the paroxysms in lead II appear to take place at the same point in diastole on each occasion.

Campbell and Elliott (1939) also considered that any irregularity, which could be detected clinically, was more likely to indicate auricular flutter.

To sum up, the rhythm of ventricular tachycardia may be regular or slightly irregular, but there is no advantage in stressing the occurrence of irregularity, since marked irregularity is an exceptional finding.

DURATION OF THE PAROXYSMS

The duration of the attacks in 13 of our patients was short, being a few seconds in the majority and less than an hour in the remainder. There were a number in whom attacks lasted several hours. The longest paroxysm appears to have been in Case 3 whose attack probably lasted over 4 weeks. He was in the hospital for one month prior to his death, and all treatment was ineffective in stopping the paroxysm. The longest case on record seems to be that reported by Elliot and Fenn (1934) in a girl, aged 19; this lasted 32 days.

FACTS AND THEORIES AS TO THE PRODUCTION OF VENTRICULAR TACHYCARDIA

When there are numerous theories and each is supported by reliable workers, it is usually safe to say that none are satisfactory and that all contain some elements of the truth. In no subject is this more apparent than in the abnormal heart rhythms. Here elaborate theories have been built upon comparatively meagre knowledge of the human heart and a large amount of experimental work on the hearts of lower animals.

The most commonly accepted explanation has been that of a "circus" movement, based upon the experimental work of Mayer (1908). He caused a contraction wave to travel round a ring of tissue, cut from the bell of a jellyfish, by producing a temporary block in one portion. Garrey (1913, 1924), Mines (1913), Lewis, Feil, and Stroud (1918), De Boer (1920, 1927), and Wiggers (1940, 1941) are some of the workers who have put forward theories on the mechanism of the circus wave and modes of re-entry of the impulse to areas that were previously refractory.

Rothberger *et al.* (1913, 1922,·1931) held that all the "ectopic" rhythms could be explained by differences in the rate of impulse formation, due to an ectopic focus beating at a rapid rate. This idea was incorporated in the theory of parasystole (Kaufman & Rothberger, 1918), in which this focus was cut off from the remainder of the heart during normal rhythm by an area of block. The theory "tachisystole" was also put forward in various forms by Herring (1917), Haberlandt (1918), and Scherf (1928).

Geraudel (1925, 1926, 1928) also held that the differences between the "ectopic" rhythms were only those of speed of impulse formation. He put forward the theory of "cardionectors," based upon the specialized blood supply to the S-A and A-V nodes and the complete independence of these nodes from one another. Any abnormal rhythm was due to the speeding up of one or the other of these two centres.

The origin of ventricular tachycardia is closely bound up with that of extrasystoles. Lewis (1925)

pointed out that patients who present paroxysms of tachycardia constantly exhibit isolated extrasystoles during slow rhythm, which are usually of a similar nature to the complexes of the paroxysms and are provoked by similar agencies and terminated by similar means. For such reasons, he believed that paroxysmal tachycardia and extrasystoles were alike phylogenetically. He summed up much of the experimental work and present-day conception of extrasystoles. "In the frog all parts of the heart muscle are capable of originating rhythmic impulses. Many parts of the mammalian heart will initiate beats under particular circumstances, but there is little evidence that those containing no special tissue can keep the heart beating rhythmically in situ. There is little evidence to suggest that extrasystoles can spring from the ventricular muscle as opposed to the Purkinje system and there is some evidence to suggest the latter as their usual starting point."

Clinically, extrasystoles and paroxysmal tachycardia are very closely related, while in the auricle, the dividing line between paroxysmal tachycardia and flutter, and flutter and fibrillation, is difficult to define. On these grounds alone, there would be ample justification for regarding the basis for all these four rhythms as essentially the same. This view has been put forward by many workers (Kauffman & Rothberger, 1917; Garrey, 1924; Wiggers, 1937; and others).

However, no one as yet has laid the foundation upon which any theory for the tachycardia can be built, for few have suggested or shown any adequate reason for the S-A node during normal rhythm or the A-V node during heart block to continue to send out impulses. To postulate other centres, as in some of the theories, seems to introduce unnecessary complications. All the theories have been built up on circumstantial evidence and, although strong and undoubtedly correct in some instances, there has never been any direct proof for any of them. The experimental work upon which each theory has been built has always called forth a certain amount of justifiable criticism from other workers in the same field. Further, there has been no very convincing evidence put forward to show why the abnormal rhythm commences, why occasionally a single beat will cause a paroxysm of fibrillation and not tachycardia, why a paroxysm once started should ever cease abruptly, or why an extrasystole should not precipitate a paroxysm of tachycardia in every case.

The basic fact, upon which the theory of the ectopic origin of the ventricular premature beat has been founded, is the aberration of the ventricular complex. Very little attention has been paid to the aberrant ventricular complex on the occasions on which it is quite certain that the impulse has reached the ventricles through the A-V node. Lewis (1911) and White *et al.* (1916, 1928) have called attention to such cases and have shown conclusively that the earlier the auricular ectopic beat, the more possibility there is for the resulting ventricular response to show some degree of aberration. The sole reason for such an occurrence appears to be the degree of prematurity, and in any tracing that shows numerous ventricular extrasystoles, it will be seen that the earlier in diastole that the beat arises, the more aberrant become the ventricular complex.

In published tracings of induced extrasystoles (e.g. Lewis, 1925), the shape of the complexes also varies with the degree of prematurity. In the examples given, no complex is the same and none arises at the same time after stimulation. While these observations in no way disprove the original contention that the extrasystoles arise from various points in either ventricle, the experiments will also support the theory that the aberrant ventricular complexes are due to stimuli arising from a single centre at various times in the cardiac cycle, possibly in the case of the ventricle, the A-V node itself.

Direct stimulation of the human heart (Barker, Macleod, & Alexander, 1930; and Lundy, Treiger, & Davison, 1939) has not clarified the position, as it is possible to produce similar shaped complexes by stimulation of given points either in the right or left ventricles.

Consideration of the causes and precipitating factors of the cases of auricular tachycardia and fibrillation makes it clear that reflex action (possibly through temporary alterations in the physicochemical state of the conducting systems and the chemical mediators of the autonomic nervous system) rather than any organic disease plays by far the major role in their production. In the cases of ventricular tachycardia, coronary heart disease is present in 80 per cent of our cases. If, however, one takes into consideration the preponderant amount of coronary heart disease that comprises the material of the laboratory of the Massachusetts General Hospital, it seems evident that coronary heart disease *by itself* can only play a minor role. Infarction of the cardiac muscle with various local upsets in the coronary circulation should provide numerous occasions for the escape of the ectopic rhythm centres and initiation of various types of local block, etc. The fact remains that it does not do so in the vast majority of cases.

In recent years, evidence has been accumulating on the supernormal phase of the cardiac cycle and its possible role in the production of abnormal rhythms.

In 1912, Adrian and Lucas applied the term "supernormal phase" to a condition occurring in injured excitable tissue. They found that there was a short period, during recovery from a previous stimulus, in which the tissue became hypersensitive to new stimuli. They also showed that this supernormal excitability of nerve tissue was accompanied by a supernormal variation in conductivity.

Adrian in 1920 again confirmed this work and showed its presence in the frog's ventricle. De Boer (1920) noted that a single stimulus, applied to a desanguinated frog's ventricle some time after the refractory period was over, caused an extrasystole, whereas a stimulus applied immediately after the refractory phase caused a " continuous circulation," though he did not postulate a supernormal phase.

In 1924, Lewis and Master were the first to apply this conception to the human heart. In one of their cases, a case of paroxysmal heart block, the P waves were only conducted to the ventricle at a phase of the refractory period which is usually totally unresponsive. This phase lay between the summit and the end of the T wave. They likened this to the supernormal phase of Adrian and Lucas. In 1925, Ashman showed its presence in the conduction tissues of the turtle and, together with Herrmann in 1926, suggested that a case of paroxysmal complete heart block could be explained by such a mechanism.

Since then a number of other cases have been described (Jervell, 1934; Luten D, & Pope, 1930; Scherf & Schott, 1939; and Kline, Conn, & Rosenbaum, 1939). Although doubt has been cast upon the interpretations of some of the tracings, it now seems to be accepted that the supernormal phase does occur at various points in the human cardiac cycle, and it may account for both A-V and V-A conduction in certain cases.

Eccles and Hoff (1934) have shown experimentally that a supernormal phase may occasionally be present in the pacemaker of the heart.

Erlanger and Gasser (1936) have shown the existence (in nerve) of certain after potentials, long after the period of excitation accompanying the propagation of the impulse, and that these potentials are associated with various phases of the recovery process. They also found that the supernormal phase which follows the relatively refractory period was associated with a negative after potential. This phase is very easily affected by many simple factors, such as asphyxia and alteration of the acid-base equilibrium. It might be noted here, in connection with the experimental production of ventricular fibrillation, that Schlapp (1932) showed that alkalosis, produced by overventilation, sensitized the ventricle to the action of adrenaline. Segers (1939), working with the frog's auricles, has also shown that the hyperexcitable phase is facilitated by adrenaline and sodium bicarbonate, and suppressed by ammonium chloride, potassium, and acetylcholine.

Gasser noted that nerves which show a marked supernormal phase were likely to respond to a single stimulus by prolonged repetitive discharge during which each succeeding discharge occurred at the height of the supernormal phase. He explained this phenomenon on an inherent residing subliminal stimulus which was thus able to give rise to spontaneous activity when the supernormal phase was present.

This reasoning has been applied to the Purkinje fibres of the heart by Goldenberg and Rothberger (1936), and it is suggested that the subliminal stimulus gives rise to an extrasystole whenever the supernormal phase occurs. By applying the idea of repetitive discharges, it is possible to suppose that an attack of paroxysmal tachycardia might occur.

Nahum and Hoff (1938, 1939) investigated the supernormal phase in higher animals, in cats, dogs, and a chimpanzee, and found that it occurred between the descending part of the T wave and the end of the U wave. They then investigated bigeminal rhythm in man and showed that in extrasystoles as a whole, the majority occurred on the descending limb of the T wave and in the area occupied by the U wave. Only a few occurred outside the supernormal area and these, they suggested, were of the nature of ventricular escape.

They point out that the ventricular conduction system possesses an inherent automaticity, usually subliminal. If, however, a marked supernormal phase develops, this latent stimulus may give rise to an extrasystole. Should the phase be continually present, bigeminy or even paroxysmal tachycardia might be produced. Even in the presence of a supernormal phase, should the internal stimulus be insufficient, no response may be expected: also should there be heightened automaticity of the conduction system, discharge would occur without the aid of the supernormal phase. Segers puts forward a similar view.

It is interesting to note that Lewis (1925) had postulated a " critical " period as an essential part of the mechanism to explain contrary effects produced by the vagus and sympathetic nerves and drugs such as chloroform, atropine, quinidine, and potassium salts.

We have been fortunate in securing a record of the onset of a paroxysm in 17 of our patients. The onset in 14 of these was at or near the end of the T wave (e.g. Fig. 8).

In Cases 21 and 23 (Fig. 13 and 12), there were a number of short paroxysms and in each the ventricular tachycardia, as measured by the Lucas comparator, started at the same point in diastole. The other three cases appeared to be initiated by an auricular complex. That these were paroxysms of ventricular tachycardia was shown by the presence of P waves at a slower rate during the paroxysm. In Case 13, the P–R interval was 0·32 sec. shortening to 0·18 sec. prior to the paroxysm, whilst in the other, Case 19, the P–R interval preceding the paroxysm was variable. In both, however, the occur-

rence of a P wave might be accounted coincidental, as the paroxysm commenced in the period of the cycle that may be associated with a supernormal phase. The auricular rate was also rapid in both. The third case showed a paroxysm beginning with a shortened P–R interval and a ventricular complex similar to the complexes seen in the Wolff-Parkinson-White syndrome (Fig. 14). It is only after this initial aberrant complex that the true paroxysm appears to begin.

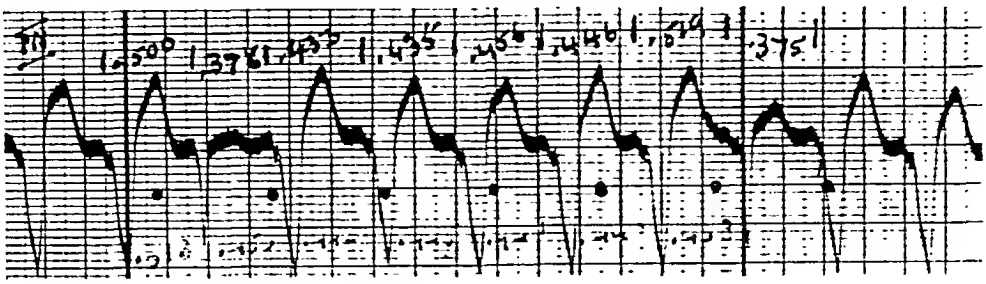


FIG. 13.—Case 21. Lead III taken during repeated paroxysms of ventricular tachycardia of varying duration: ventricular rate 140 and auricular rate 120. Comparator measurements made as to the time of onset in four successive paroxysms, were probably identical, 0·378, 0·376, 0·375 (the last two shown in the figure), and 0·373 sec.

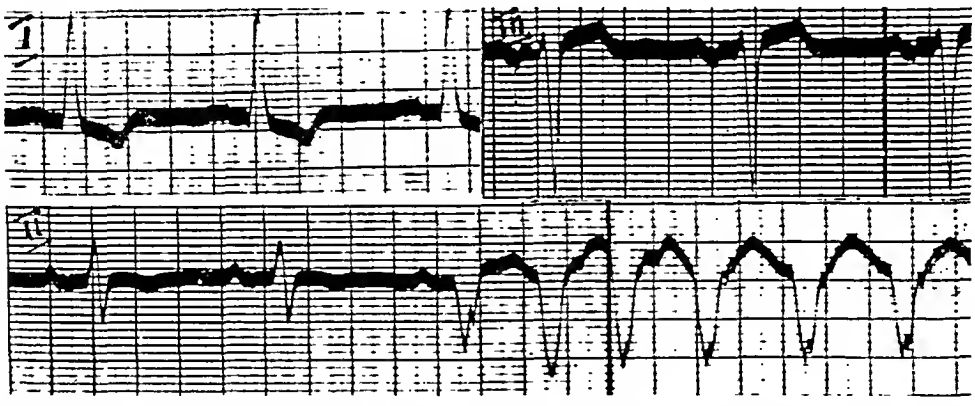


FIG. 14.—Case 10. Leads I and III (above) show normal rhythm with a P–R interval of 0·21–22 sec. Lead II (below) shows the onset of a paroxysm of ventricular tachycardia. The paroxysms is preceded by a P wave and a shortened P–R interval of 0·18 sec. The first ventricular complex appears to be different from the remainder of the paroxysm.

In Cases 22 and 24, the presence of a short P–R interval and slurred QRS complex was noted in the breaks in the tachycardia for one and two beats before reverting to the paroxysm again (Fig. 1). These findings suggest an abnormal excitability at the A-V node, and support rather than refute the hypothesis that a supernormal phase of the bundle and A-V node supplies the conditions for the onset of paroxysmal tachycardia.

To sum up then, there is evidence accumulating to suggest that extrasystoles can occur during the supernormal phase of a site of stimulus formation: when this happens, the complex is of abnormal type and in classical terminology would be designated as a right or left ventricular extrasystole. This phase is dependent upon factors that are essentially similar to those which determine the onset of paroxysms of tachycardia (changes in general metabolism, adrenaline, acetylcholine, potassium, etc.). This fact, together with the usual time of onset of the paroxysms, seems to offer some evidence in favour of the " supernormal phase " theory of paroxysmal tachycardias. There appears to be no necessity to postulate centres for the source of the ectopic rhythms other than the A-V node and the bundle, since aberration of the complexes are equally explicable on the basis of prematurity alone as by origin from ectopic focus.

At the moment, however, the conception of " re-entry " of the original stimulus through an area that was refractory at first, particularly as put forward by Wiggers (1940, 1941), is the most generally accepted explanation of extrasystoles, tachycardia, and the inception of circus movement.

Ventricular Paroxysmal Tachycardia with Alternating Complexes

There were four cases in this series showing alternation of the ventricular complexes (Fig. 15). Three of them (Cases 1, 9, & 24) have previously been reported. Three of the four had severe coronary disease, while the fourth (Case 24) had only very slight alternation and had a heart otherwise normal.

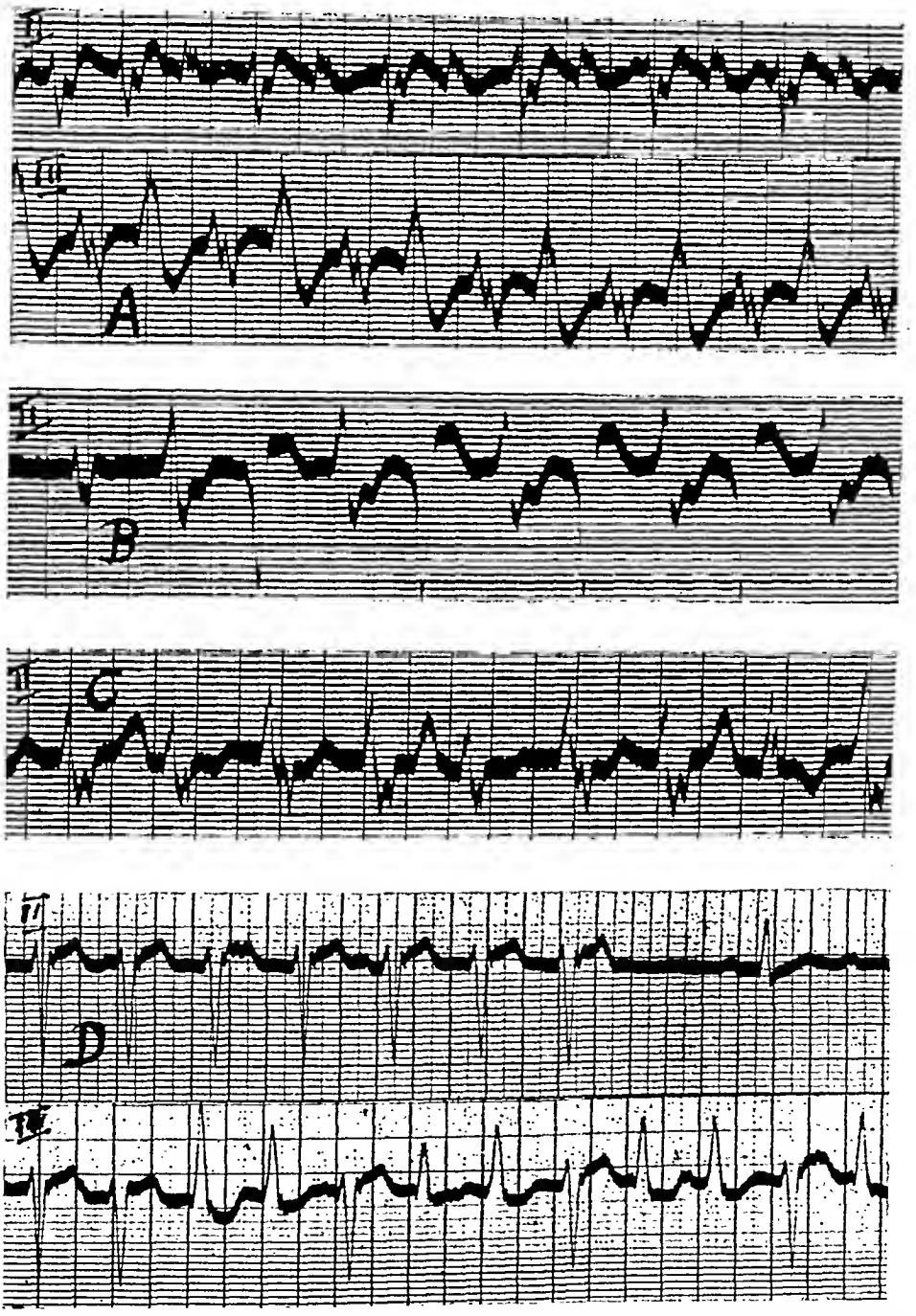


Fig. 15.—(A) At the top, leads II and III (Case 1), and (B) lead II (Case 9) show well-marked alternation. (C) Lead II (Case 24) shows very slight alternation. Electrocardiograms from these three cases have been published more fully elsewhere. (D) Leads II and IV (Case 2) shows the end of a paroxysm, and in the second strip, regular alternations of the ventricular complex. P waves are well shown.

The three cases with coronary heart disease died within a few days, while the fourth was still alive recently, twelve years after the electrocardiogram in question was taken. Digitalis had been given in excessive doses to two cases while it may or may not have played a part in the third case with coronary disease.

Various hypotheses have been put forward from time to time to explain the alternation. The tachycardia may arise from a single centre above the bifurcation of the bundle of His and the alternation may be the result of changing right and left branch block (Luten, 1924). The Purkinje fibres themselves may be refractory in alternate ventricles with successive beats so that alternate dextro- and lævo-cardiograms preponderate (Marvin, 1928). The alternation may arise as the result of the interplay of two separate rhythms (Marvin); and finally Palmer and White suggested the interplay of two separate circus movements in the ventricular muscle in alternate directions, but arising from the same site (figure of eight circus).

In several reported cases not only is there alternation in the complexes but also in the time intervals between the complexes. For example, Palmer and White carried out careful comparator measurements in two of the cases that are included in this group. The measurements they produced are striking in showing this alternation, and on this account they considered that alternation of the right and left branches was improbable owing to the difference in timing of the two types of complex.

It is possible, however, that such variations may be due to the inability to measure comparable points on the successive complexes. Neither the onset nor the peak of the R wave is identical in timing in two successive but different complexes. The beginning of the ventricular complex would be the ideal point to take comparator measurements from, and this is impossible to determine without the use of simultaneous leads. White, Leach, and Foote (1941) have shown conclusively that the beginning of the QRS complexes are frequently isoelectric in one of the leads. Marvin (1928) on the basis of irregularity of the timing of the complexes suggested that this indicated that the pacemaker must reside within the ventricles, and supposed that the resulting irregularity of the complexes was due to the varying time relations between the dextro- and lævo-cardiograms. The criticisms as to measurements may be applied to his tracings. It is probable that in all these cases, in spite of apparent variation in time intervals, the beats are regular.

Normal sino-auricular rhythm with alternating bundle branch block has been reported (Korns, 1922; and Scherf & Kisch, 1939). Since alternation of the ventricular complexes can take place in response to an impulse of supraventricular origin, and since the timing of the onset of the ventricular complexes has not yet been satisfactorily determined, Luten's explanation still seems the most rational. He wrote, " Digitalis intoxication results in a tachycardia which originates at or near the bifurcation of the main stem of the bundle. The action of the drug has also impaired to a considerable extent the conductivity of the bundle branches. An impulse is then transmitted over one (the right) branch but finds the other (the left) for the most part unable for the moment to transmit it. A small strand in the impaired left, however, does transmit the impulse but at a slower rate. This gives the picture of defective branch conduction. The next rhythmic impulse finds the bulk of the left branch restored and ready for conduction, but the bulk of the right branch has not yet recovered and so fails to transmit the impulse." Marvin (1928) had criticized such an idea on the basis of finding in one of his cases permanent bundle branch block, stating that in such a case, two centres would have to be present with one below the site of the branch block. Yater (1938), however, has shown that in such cases both bundles are severely damaged and that the electrocardiographic findings are merely an index of which branch is the most severely affected. Scherf and Kisch (1939) also believe that some, if not all, of their 18 cases can be explained by variations in conduction of impulses arising at a single point.

Therefore, on account of the reasonings we have already given, it is possible to suppose that the centre for ventricular paroxysmal tachycardia with alternating complexes lies in the bundle of His and in fact may be situated in the A-V node itself.

Prognosis

For the estimation of prognosis, the cases must be divided into two groups, those with organic heart disease and those with apparently normal hearts.

The occurrence of ventricular tachycardia in organic heart disease is a serious prognostic sign. Strauss (1930) found that of 50 cases with serious organic heart disease, 40 were dead within three hours to six months of the onset of the tachycardia, with an average duration of life of 24 days. The great majority of these received no specific medication.

The French workers, whose views have been well summarized by Froment (1932), hold that there are two types, a benign type of repeated ventricular extrasystoles occurring in young subjects (e.g. Cases 24 & 27); and the commonest type, a terminal or pre-fibrillation type which is the forerunner of death.

In our group of 21 eases of eoronary heart disease, there were four still living at the time of writing. Two of them were extremely active, the time sinee the first paroxysm of tachycardia being two years in eaeh easc. Of the other two eases, one was a semi-invalid, four months aftcr the occurrenee of the paroxysm, and thc other was eripplcd with vaseular diseasc of the legs and had only just been diseharged from thc hospital four weeks after the taehycardia.

In our remaining 17 eases of coronary heart disease, death oeeurred within periods ranging from a few hours to eighteen months. Of these, there again seemed to be two groups, the one slightly larger comprising the patients dying within the first three weeks after the event, and the other in which they reeovered for a while from that particular crisis and died some months later, in some cases suddenly and unexpeetedly. While somc of the first group would have died as a result of their eoronary thrombosis, onc or two might perhaps have survivcd a few months longer had treatment with quinidine or quinine been instituted. The exaet length of survival can be seen in the appendix. The three cascs with alternation of the ventrieular complexes and eoronary disease all died within two weeks. This is in aeeord with the experienee of reported cases.

Thcrc arc five cases of otherwise normal hearts in our group. Two of these were known to be living and well (Cases 23 & 25) at two and nine years respectively after the deteetion of the tachycardia. Case 26 had not been traeed. Case 24 was alive in 1937, 12 years aftcr the detection of the arrhythmia and 25 ycars after the probable onsct; we werc unable to get in toueh with him more recently. Case 27 probably has an interventricular septal defeet and also shows short P–R intervals and wide QRS complexes during normal rhythm; shc was alive and well 14 years after the onset.

Case 15 might possibly throw doubt upon the diagnosis of the five irritable normal hearts. This patient, a woman aged 42 years, was diagnosed as having an irritable normal heart, but follow-up study revealed that she died three to four years later. The mode of death was not known but she has been elassed as a case of probable coronary heart disease elsewhere in this paper. She was under observation for one year, during which treatment had little effeet upon the frequency of the attacks. Oeeasionally similar cases have come to autopsy, e.g. Seherf's patient (MeKinnon, 1934) who had paroxysms over five years, died with eongestive failure, and had a heart in which there was no demonstrable disease. Campbell and Elliott (1939, p. 147) reported two similar cases. In these, both males aged 17 and 21 years, the paroxysms had been present over periods of five years and six months respectively before sudden death oeeurred.

The prognosis then is generally poor though exceptions are met with. A few cases with organic disease will manage to survive and young patients with apparently normal hearts have a good chanee of lengthy survival.

Treatment of Paroxysm

Quinidine appeared to help the two patients with coronary heart disease who lived longest and at last aecount were still actively working. In two cases it seemed to eounteract the effect of digitalis very rapidly, although not averting the fatal issue in either case. No effect could be obtained in Case 3 who was given a minimum dose of 18 grains daily and a dosage pushed to toxic levels on three oeeasions during the month he was in hospital.

Earlier writers (Levy, 1922; Drury *et al.*, 1922; and Levine, 1927, etc.) stressed the possibility of producing ventrieular fibrillation with quinidine. Cases, too, have been reported in which the ventricular tachycardia only ceased on its withdrawal. Such cases, however, are rare and some of the examples reported have been attributed to quinidine wrongly. Occasionally perhaps the heart is in such an irritable state that any cardiac drug will provide the necessary stimulus for the tachycardia. We believe then, that the possibilities of inducing ventricular fibrillation should never weigh against the use of quinidine.

In our group of cases quinidine in various dosagc has been given only by mouth. For example, Case 19 received 3 grains at half-hourly intervals for five doses before the rhythm became normal after an attack which lasted six hours. Quinidine may be given in 3 to 6 grain doses every two to three hours until either restoration of normal rhythm occurs or signs of intolerance develop. The necessary dose shows a great variation from patient to patient. When the rhythm does become normal, a daily maintenance dose should be continued for three to four months at least. There appears to be no contra-indication to the prolonged administration of quinidine. Case 21 and Case 23 both took 3 to 6 grains of quinidine daily for over two years and have shown no ill effects from the drug; other patients have taken even larger doses of the drug for many years without harm.

Treatment with intravenous injections of quinidine has been reported on favourably by Hepburn and Rykert (1937). They treated 9 cases with intravenous quinidine, 50–60 grains dissolved in 500 c.c. of 5 per cent glucose and given at a rate of 100–120 c.c. an hour. They pointed out that of these nine cases six were alive at the time of writing, for period up to four years since the tachycardia,

whereas only one out of nineteen cases who were not so treated lived longer than 15 days. Others (Bunn, 1932 and Battro, 1937) have also had good results.

The most convenient and effective method of stopping ventricular tachycardia that has proved refractory to drugs by mouth is, however, the use of quinine dihydrochloride by intramuscular injection, 5 c.c. of aqueous solution containing 7½ grains (0·5 gram) given every two hours until normal rhythm is restored or severe cinchonism results (Riseman & Linenthal, 1941).

Mecholyl (acetyl-B-methylcholine chloride) has been used with good results in paroxysmal auricular tachycardia, and in such cases, ventricular standstill is not uncommon. Mecholyl has also been used experimentally by Nahum and Hoff (1934) to prevent the onset of ventricular tachycardia induced by the action of benzol, adrenaline, and electrical shocks. It is not surprising, therefore, that it has been used for the treatment of ventricular paroxysmal tachycardia; Stern (1937) reported failure in two cases so treated.

It has been suggested (Hall, 1939), however, that acetycholine causes coronary artery spasm and certainly in some patients, its administration causes symptoms well-nigh indistinguishable from those of angina pectoris. There is clearly an element of danger in using such a drug in hearts of the sort usually found in patients with ventricular paroxysmal tachycardia. We believe, therefore, that if this drug must be used, it should be given only to young patients (e.g. Cases 24, 25, & 27) who have otherwise normal hearts.

There will remain a few patients in whom the attacks of ventricular tachycardia can be controlled only by the administration of full doses of both digitalis and quinidine (e.g. Scherf and Kisch's case).

Summary

We have reported 27 cases of ventricular paroxysmal tachycardia: 24 of these were found in a review of some 51,000 plates and films taken on about 25,000 patients in the Cardiographic Laboratory of the Massachusetts General Hospital over a period of 25 years from 1914 to 1939.

The criteria for diagnosis were the electrocardiographic findings. Fulfilment of any one of the following four points justifies the diagnosis.

1. The presence of P waves at a slower rate than that of abnormal QRS waves during a paroxysm of tachycardia.
2. A paroxysm of abnormal ventricular complexes, that is, three or more, occurring during auricular fibrillation.
3. The onset of the tachycardia with an abnormal ventricular complex.
4. Close resemblance of the complexes of ventricular premature beats to the complexes occurring during paroxysmal tachycardia.

Coronary heart disease was present in 22 of our 27 cases, 4 had apparently normal hearts, and 1 was thought to have a congenital ventricular septal defect. There were 17 males and 10 females, the youngest being aged 18 years and the oldest 81 years.

Digitalis had been administered to 13 of the 27 cases before the onset of the tachycardia. It was probably the chief ætiological factor in at least 5 of these cases.

It is suggested that abnormalities of the ventricular complexes of premature beats are responses to stimuli arising in the A-V node or bundle or main branches at a point in the cardiac cycle when the conducting tissues are still partially refractory. The onset of ventricular tachycardia was generally in the part of the cycle that has been associated with the supernormal phase. The mechanism of ventricular tachycardia with alternating complexes may be due to abnormalities in conduction along the bundle branches in response to impulses arising in the A-V node.

The prognosis is generally, but not always, poor. Only two patients with coronary heart disease survived longer than two years after the first attack. Five patients with hearts otherwise normal have survived to date, periods varying from two to fifteen years.

Quinidine or quinine should be used in adequate dosage in the treatment of the attack, being given either by mouth, intramuscularly, or intravenously. Quinidine sulphate is most conveniently given by mouth in the dosage of 6 to 9 grains every 2 hours for 5 to 6 doses under close observation and preferably with electrocardiographic control. If quinidine fails, quinine dihydrochloride, grains 7½ subcutaneously, every 2 hours, is recommended to stop the paroxysm and even to save life. A daily maintenance dose of quinidine by mouth (3 grains of the sulphate, 4 times a day) may be continued for prophylactic purposes for an indefinite time.

Appendix of Case Notes

In all these cases, the age given has been the age at death or, in the cases of those living, the age at the completion of the survey. EC. is used for electrocardiogram.

Case 1 (Fig. 15 B). A man, aged 50 years, had angina pectoris for three years and an attack of coronary thrombosis ten days before admission to hospital. There was slight congestive failure and a pulse rate of 190 with a B.P. of 140/105. On admission, he was given large amounts of digitalis, 27 grains in all, but died 40 hours after entry. Autopsy showed a heart weighing 545 g. with signs of fresh infarction at the apex of the left ventricle; a recent thrombus was present in the descending branch of the left coronary artery.

Case 2 (Fig. 15 D). A man, aged 80, was admitted in marked congestive failure. B.P., 160/90. Fairly rapid digitalization was carried out, 24 grains in 84 hours in this man who weighed but 125 pounds. The presence of ventricular tachycardia with alternating complexes at the end of this period was noted. EC., slight prolongation of the P–R interval and slight sagging of the S–T segments in leads II and III gave some indication of the digitalis effect. Death occurred 48 hours later. At autopsy the heart weighed 575 g. and showed diffuse coronary sclerosis.

Case 3 (Fig. 16). A man, aged 48, was treated for hypertension and coronary heart disease, following an attack of coronary thrombosis three years previously. After a cold, he developed congestive heart failure and ventricular tachycardia. Digitalis, 20 to 30 minims, t.i.d., had been administered

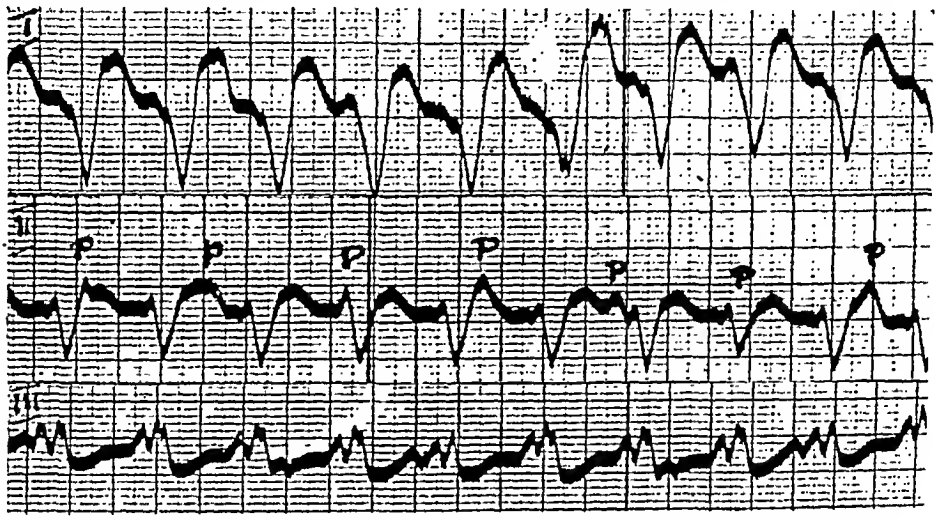


FIG. 16.—Case 3. Ventricular tachycardia at a rate of 140; auricular rate, 95. This attack lasted for more than twenty-eight days, probably for six weeks, terminating in the patient's death.

for one month prior to admission. No treatment, even quinidine in toxic doses, availed to stop the rhythm. He died one month after admission when digitalization was again being attempted. Ventricular tachycardia had been present for about six weeks. Autopsy showed a heart weighing 700 g. Most of the anterior wall of the left ventricle and lower part of the interventricular septum had been replaced by fibrous tissue.

Case 4. A man, aged 70, who had stopped work a few weeks previously owing to shortness of breath, was admitted to hospital with Cheyne-Stokes breathing and marked congestive failure. EC., ventricular tachycardia. He died 12 hours after admission. Digitalis, 6 grains, was given in hospital but the dosage given over the previous three weeks was not known. Autopsy showed a heart weighing 700 g. with diffuse coronary atherosclerosis.

Case 5. A man, aged 60, had had large doses of digitalis, 4·5 grains daily, for one week which should have been enough to complete digitalization, but he continued with 3 grains daily for a further week at the end of which time he had diarrhœa and attacks of ventricular tachycardia. A further 6 grains were given in hospital. He died suddenly and unexpectedly 20 hours after admission, quite possibly the result of ventricular fibrillation. His heart weighed 680 g. and showed moderate left ventricular hypertrophy and diffuse coronary atherosclerosis. EC., very little evidence of digitalis intoxication.

Case 6. A man, aged 55, was, compared with some of the other cases, in very mild heart failure. Massive doses of digitalis, however, had been given on admission, 54 gains in 120 hours, at the end of which time he showed ventricular tachycardia. Digitalis had been continued in spite of the continuance of this arrhythmia until his death seven days later. Shortly before death an attempt was made to control the attacks with quinidine. The effect of the digitalis on the EC. was to produce periods of bradycardia during which there was complete A-V dissociation, the S–T segments showing very little deviation.

Case 7. A man, aged 53, was admitted for fainting attacks following an attack of abdominal pain two months previously. A diagnosis of coronary thrombosis and attacks of ventricular tachycardia was made. He died 18 months later while taking an automobile test. No autopsy.

Case 8. A man, aged 57, had suffered with symptoms of hypertensive heart disease for over a year. He was admitted to the hospital after the onset of auricular fibrillation and an exacerbation of his symptoms: B.P., 220/120. He was kept on a maintenance dose of digitalis with rest periods and died fourteen months later in congestive failure. No autopsy.

Case 9 (Fig. 15 B). A man, aged 45, had been admitted to the hospital seven years previously with congestive failure, and recently with auricular fibrillation and congestive failure of two weeks' duration; he had been in fairly good health since his first admission; B.P., 130/100. He was given 30 grains of digitalis over the first 48 hours when the EC. revealed ventricular tachycardia with alternating complexes. He developed pneumonia and died 7 days later. No autopsy.

Case 10 (Fig. 14). A man, aged 66, was treated for hypertension and coronary heart disease with a daily maintenance of digitalis for four years prior to his death, being admitted to hospital on three occasions for congestive failure. EC. showed ventricular tachycardia during his last admission to hospital, 8 months prior to his death. No autopsy.

Case 11. A man, aged 49, was admitted complaining of abdominal pain for which an exploratory laparotomy was performed. He then developed congestive heart failure and cardiographic changes of coronary thrombosis. Following digitalization, 42 grains in 14 days, he had an attack of ventricular paroxysmal tachydardia of 6 to 8 hours' duration. Digitalis was continued with normal maintenance dose. He died 8 months later. No autopsy.

Case 12. A woman, aged 44, developed a pelvic abscess, following an operation for hyperthyroidism and a diagnostic dilatation and uterine curettage. During convalescence she had a cerebral embolism, and an EC. during this upset showed the presence of ventricular tachycardia. She died a few hours later. No autopsy.

Case 13. A man, aged 60, was first seen by us in a state of digitalis intoxication, having for the past three-and-a-half months taken 1·5 grains three or four times daily. When seen he had been semi-conscious and delirious for nearly four days while his pulse, normally 70, showed numerous runs of tachycardia at the rate of 150. The ventricular tachycardia showed no signs of stopping after omitting the drug for two days but stopped immediately with quinidine. The EC. then showed prolonged A-V conduction, 0·32 sec. (six months previously, 0·24 sec.). He was thought to be well on the way to recovery when he developed signs of lung involvement. He died six days after the cessation of digitalis.

Case 14 (Fig. 17). A woman, aged 62, had stopped working twelve months previously owing to shortness of breath. One week prior to entry, she had had an attack of fainting and had been weak

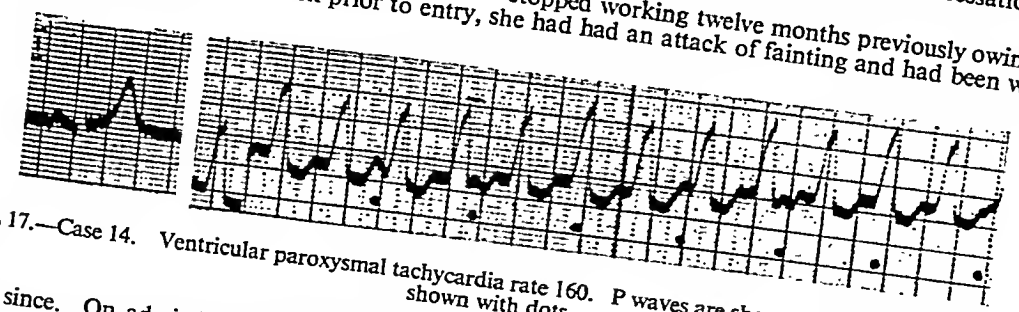


FIG. 17.—Case 14. Ventricular paroxysmal tachycardia rate 160. P waves are shown at a rate of 100, and are shown with dots.

ever since. On admission she had congestive failure and a rapid pulse rate which was shown by EC. to be ventricular tachycardia. Digitalis given after onset, 36 grains in 4 days, and thereafter maintenance dose of 1·5 grains. Follow-up study two years later revealed that she had died but the date and details were unknown.

Case 15. A woman, aged 42, was admitted to the hospital on account of a neck swelling and a feeling of compression there, of one year's duration, and palpitation of six months' duration. There was a goitre but no signs of hyperthyroidism were detected; EC. showed ventricular paroxysmal tachycardia. Hemi-thyroidectomy was performed for pressure symptoms. She died more than eighteen months later; the details were unknown.

Case 16. A woman, aged 52, had symptoms of hypertension and coronary heart disease for one year. B.P., 210/100: taking small and varying quantities of digitalis for the previous five months. EC. whilst in hospital showed attacks of ventricular tachycardia. She made very little improvement and died at home three months later. No autopsy.

Case 17 (Fig. 7). A man, aged 54, had suffered with auricular fibrillation for seven years, for which he had been taking small quantities of digitalis. His symptoms had been more marked over the previous five months; EC. showed short runs of ventricular tachycardia. His subsequent fate is unknown.

Case 18 (Fig. 10). A woman, aged 59, had been taking 2 to 3 grains of digitalis daily for a year and then three weeks previously had increased her dosage to 6 grains daily. She was admitted in marked congestive failure, complaining of much blurring of vision, weakness, and marked loss of appetite. B.P., 160/110. EC. showed ventricular tachycardia and markedly depressed S–T segments in leads II and III. She improved somewhat with diuretics, on the omission of digitalis. She died at home about four weeks later.

Case 19. A man, aged 63, had suffered with angina pectoris for 18 years and was admitted owing to an increase of symptoms and tachycardia for the previous three weeks. Following 1·1 gram of digitalis over 36 hours, he developed ventricular tachycardia which eventually was controlled by large doses of quinidine, a maintenance dose of which for the next three months completely controlled the arrhythmia. On re-admission, 18 months later, another paroxysm of ventricular tachycardia of twenty hours' duration was again controlled by quinidine. Digitalis probably played no part in this case.

Case 20. A woman, aged 72, had been treated for arthritis for many years. Four years previously she had been admitted to the hospital with coronary thrombosis. Following an increase in her cardiac symptoms, she was readmitted. EC., auricular fibrillation with short runs of ventricular tachycardia. The tachycardia was noted again following digitalization. She was still alive four months later, taking a daily maintenance dose of digitalis.

Case 21 (Fig. 13). A man, aged 72, had suffered with a duodenal ulcer for over 30 years. Two years previously he suffered a coronary thrombosis and during convalescence he developed ventricular tachycardia. Digitalization made the tachycardia more troublesome. On omitting it and giving a daily dose of quinidine, no further trouble was experienced. He was still alive two years after his heart attack.

Case 22 (Fig. 1). A man, aged 71, had been known to have had coronary heart disease and intermittent claudication of the legs for the previous four years. He was admitted with an occlusion of an artery of his leg, and showed slight congestive heart failure and an EC. revealed ventricular tachycardia. Digitalization was carried out without any ill effects, 33 grains in four days followed by maintenance dose of 1½ grains. He was discharged home much improved.

Case 23 (Fig. 12). A woman, aged 46, had undergone X-ray treatment for hyperthyroidism apparently with benefit twenty years previously. Three years ago she again attended the hospital on account of dizziness and giddiness. The heart was thought to be slightly enlarged and an EC. showed the presence of attacks of ventricular tachycardia. Paroxysmal tachycardia was thought to be the cause of her faint spells. She has, therefore, taken a maintenance daily dose of 3 to 6 grains of quinidine with great improvement in her symptoms and lessening of the attacks of tachycardia. She is now well.

Case 24 (Fig. 8 & 15 C). A man, aged 30, was first seen by us at the age of 18 years owing to repeated attacks of tachycardia which had been present since childhood. His father, a physician, had observed them at the age of 5. His only symptom had been a consciousness of almost continuous spells of rapid heart action. Examination did not reveal any obvious abnormality while an EC. showed numerous short runs of ventricular tachycardia. Treatment did not appear to improve his condition.

Case 25 (Fig. 18). A woman, aged 42, began to have attacks of paroxysmal tachycardia eight years ago. They have been and are still frequent and fairly persistent. On examination she has always

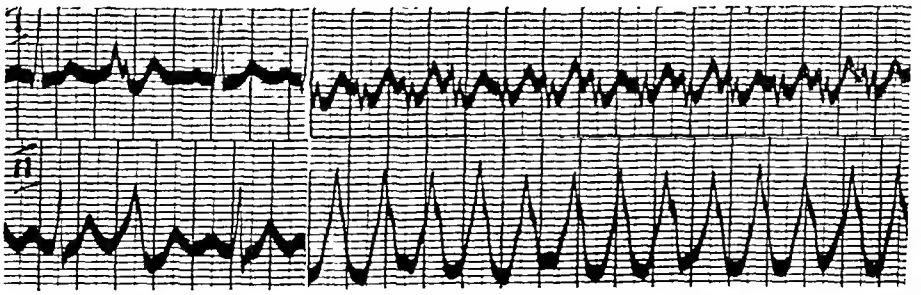


FIG. 18.—Case 25. Leads I and II. Ventricular extrasystoles are shown during normal rhythm. The ventricular complexes during the paroxysms are sufficiently similar to those of the extrasystoles during normal rhythm to indicate the ventricular origin of the tachycardia.

appeared to be perfectly normal. B.P., 130/80; EC. showed that the attacks were ventricular in origin.

Case 26 (Fig. 11). A woman, aged 21, was admitted to the hospital for investigation of her thyroid. She had lost weight and had started to have attacks of rapid heart action six weeks previously. EC., paroxysmal ventricular tachycardia. No organic disease was discovered. Her subsequent history is unknown.

Case 27 (Fig. 2). A woman, aged 32, had for the past fourteen years had spells of rapid regular racing of the heart, lasting up to 52 hours. The EC. showed a short P–R interval, a widened QRS complex, and runs of ventricular tachycardia. Examination suggested the presence of an interventricular septal defect. She still has frequent attacks of tachycardia but is otherwise well.

Five cases with Paroxysmal Tachycardia of Doubtful Origin

Case 28 (Fig. 3 A). A man, aged 40, had had attacks of paroxysmal tachycardia for 25 years, almost constant at times. Treatment had little effect. Physical examination showed nothing abnormal.

Case 29 (Fig. 3 B). A man, aged 39, was first seen 16 years ago when he gave a history of having developed pain, dyspnœa, and vomiting after a long quick run. B.P., during the attack, 70/55, and pulse rate 210. Examination was otherwise normal. He is at present well, suffering only an occasional bout of palpitation.

Case 30 (Fig. 3 C). A man, aged 33, was admitted in an attack of tachycardia, paroxysmal in type. Physical examination was negative. Follow-up study ten years later revealed that he had died, but the details and date are unknown.

Case 31 (Fig. 5). A man, aged 25, had developed tachycardia seven years previously while playing a strenuous game of tennis. This attack lasted three days before it was stopped by quinidine. Examination was normal. He has had no more attacks since that time, and is extremely fit and active.

Case 32. (Fig. 3 D). A man, aged 26, was admitted to the hospital following a collapse during a paroxysm of tachycardia. He was also suffering from acute gonococcal urethritis. Physical examination also revealed well-marked mitral and aortic rheumatic heart disease.

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PARTIAL HEART BLOCK WITH DROPPED BEATS

BY

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Partial heart block with dropped beats is, in my experience, generally found during acute infections or after too much digitalis. This is such a contrast with the ætiology of complete heart block, that it seems worth analysing a series of cases with all degrees of heart block, to see what association there is between partial block with dropped beats and complete block, and to define more precisely the conditions producing the former. The second part of the paper deals with the progressive changes found in the P–R intervals before and after the dropped beat.

I. Clinical Observations

There were 29 patients who had partial heart block with dropped beats without any higher degree of block. This was nearly one eighth of the total number ; but the condition is noticed less frequently than this would suggest, because generally it persists for a few days or weeks only, while in other types the degree of block is likely to be of long duration so that the patient is seen again, perhaps over a long period.

The occurrence of dropped beats is nearly always very transient, and most often due to an acute infection or to treatment with digitalis. The 11 cases in this last group have already been discussed (Campbell, 1942) and in 6 of them infection was an additional factor. In the 18 where it was not due to digitalis, 6 had acute rheumatism and 6 had other infections, most often acute tonsillitis that did not appear to be a manifestation of rheumatic fever. Thus, 12 of the 18 had active infection at the time : most of these were young adults. In the remaining 6, who were nearly all older patients, there was no evidence of an active infection, and even when the condition was transitory it seemed to be a stage in their chronic disease or was observed at times without any obvious reason.

There were a further 9 cases, making 38 in all, where there was at one time partial heart block with dropped beats, and at other times a higher degree of block, such as 2 : 1 or even complete block (see Table I). Only 2 of these belonged to the group with active infection, and 7 to the older group with chronic disease.

TABLE

Ætiology of Cases with Dropped Beats

Ætiology	Partial heart block with dropped beats only		Partial block with at other times higher grades of heart block	Total
	caused by digitalis	other causes		
Acute rheumatism ..	2	6	1	9
Other acute infections, mainly tonsillitis ..	1	6	1	8
Chronic myocardial disease*	8†	6	7	21*
Total number of cases ..	11	18	9	38

* Of the 21 cases, 3 were rheumatic ; the remainder in each group were almost equally distributed between (*a*) hyperpiesia, (*b*) coronary atheroma, and (*c*) heart failure or a large heart without proof of (*a*) or (*b*).

† Infection was an additional factor in 3 of these.

Ætiological Factors

1. *Active infection.* (*a*) *Acute rheumatism.* There were nine patients in this group. They did not seem to be quite representative of average cases of this disease, as a boy of 18 with a typical first

attack (Case 13) was the only one under 24 years of age. Three had pericarditis. The first started with pericarditis and partial heart block and developed aortic incompetence (Case 1). The second had pericarditis and joint changes that were in some ways less like rheumatic than rheumatoid arthritis, and no evidence of valvular disease (Case 21). The third developed complete heart block at the start of a recurrent attack of rheumatic fever (she already had aortic incompetence) ; this lasted for a week and was followed by partial block, sometimes with dropped beats, sometimes 2 : 1, and this persisted for three months : in spite of this she made an excellent recovery and was in good health twelve years later with very little change in these intervening years, although she did a fair amount of work running her father's house (Case 113, Campbell, 1931). Another man, aged 51, also escaped without permanent changes after a classical severe attack—the first and only other attack having been 38 years before (Case 22).

There was nothing special to say about the remaining patients, all of whom had established valvular disease before the attack in which dropped beats were observed, except that in three the recurrence causing the dropped beats seemed in other ways a trivial one. The cases are summarized in Tables II and III, and those caused by digitalis in Table II of the previous paper.

As has been noted in other series, the aortic valve was affected more frequently than in an average series of rheumatic cases, the figures being : aortic disease, 2 cases ; aortic and mitral disease, 1 ; mitral disease, 4 (in 2 the mitral involvement was slight) ; no valvular disease, 2 cases.

TABLE II

DROPPED BEATS, BUT NO HIGHER DEGREE OF HEART BLOCK (18 CASES) *

Case No.	Sex and Age	Diagnosis	P–R interval		
			with dropped beats	without dropped beats†	after recovery
		Acute rheumatism			
1	m.25	Rheumatic pericarditis ; developed aortic incompetence	—	—	0·19
10	f.30	Aortic and mitral disease ; recurrent rheumatism	0·28–0·40	0·32	0·21
13	m.18	Acute rheumatism (first attack)	0·24–0·41	—	0·16
15	f.34	Mitral systolic murmur; recurrent rheumatism	0·24–0·32	0·28	0·18
21	m.30	Pericarditis and acute arthritis	0·45–0·48	0·47	0·18
22	m.51	Acute rheumatism (second attack)	—	0·34	0·16
		Other infections			
5	f.18	Acute tonsillitis; early tuberculosis of lung	—	0·32	0·21
17	f.23	Tonsillitis; previously erysipelas	—	0·32	0·16
23	f.21	Quinzy and hyperthyroidism	0·20–0·40	0·36	0·20
25	f.45	Thyrotoxicosis; acute tonsillitis	0·28–0·38	0·26	0·18
29	m.50	Recurrent dysentery; later slight sore throat	0·35–0·42	0·42	(0·28)
20	m.29	Tuberculosis of lungs; nephritis; enlarged heart; dextrocardia	0·29–0·56	0·56	—
		Chronic Rheumatic			
7	m.22	Mitral stenosis ; ? gonococcal myocarditis	0·20–0·36	0·36	—
14	m.52	Rheumatic aortic incompetence	0·28–0·44	0·28	—
		Myocardial			
3	m.61	Atherosclerosis; B.P. 180/100	0·25	0·25	—
6	f.70	Cerebral thrombosis; heart failure	0·24–0·38	0·24	—
16	m.80	Coronary atheroma	—	0·30	—
24	m.66	Enlarged heart; B.B.Bl.	0·24	0·24	—

* Cases where the dropped beats were due to digitalis have not been included here (see Table II of the previous paper).

† In most cases the P–R interval when the heart block is latent is almost the same as the first P–R with a response at a time when there are dropped beats, but in cases 7, 20, 21, 23, and 29 it is almost the same as the last P–R interval before the dropped beat.

TABLE III

CASES WITH DROPPED BEATS AND AT OTHER TIMES A HIGHER GRADE OF BLOCK (9 CASES).

Case No.	Sex and Age	Diagnosis	P–R interval			Presence of complete heart block
			with dropped beats	without dropped beats *	with 2 : 1 heart block†	
		Acute rheumatic				
113	f.25	Acute rheumatic carditis; aortic incompetence	0·18–0·25	0·16 ‡	0·19	+
		Other infections				
109	m.55	Congestive failure; ? infective endocarditis	0·20–0·30	0·17	0·19	—
		Chronic rheumatic				
107	f.42	Rheumatic mitral endocarditis ..	0·29–0·40	0·28	{ 0·24 0·28 }	+ (once)
		Myocardial				
103	f.66	High B.P. (250/115)	0·21	0·21	0·21	+
104	m.64	Early congestive heart failure	0·29–0·41	0·34	0·31	?+ (once)
110	f.62	Coronary atheroma	0·23–0·28	0·23	0·23	—
112	f.72	High B.P. (175/90)	0·24–0·32	0·29	0·23	—
117	m.56	Enlarged heart nephrectomy for tumour	0·26–0·30	—	0·26	—
119	m.49	Coronary disease; ? atheromatous, ? syphilitic	0·28–0·40	0·40	0·40	+

* The P–R interval of latent block is almost the same as the first P–R interval with a response, except in Cases 104, 112, and 119.

† The P–R interval with 2 : 1 heart block is almost the same as the first P–R interval with a response, except in Case 119.

‡ This was obtained at a later period, after recovery.

1 (*b*). *Other active infections, mostly tonsillitis.* There were eight cases in this group. Two of them were specially important because the dropped beats were caused by ordinary attacks of tonsillitis in patients with normal hearts. They are therefore described more fully below. It has been suggested that a prolonged P–R interval in a young person is pathognomic of acute rheumatism, but there was not the slightest reason to suspect that these patients or their attacks of tonsillitis were rheumatic.

In three others, throat infections and thyrotoxicosis were associated (see p. 58). A sixth had congestive heart failure with some infection, probably infective endocarditis (Case 109). The seventh, having had bacillary dysentery several years before, was recovering from a relaspe and had a slight sore throat soon after the dropped beats had been found rather unexpectedly (Case 29). The eighth had advanced tuberculosis of the lung and a large white kidney, and died three weeks later with suppurative parotitis (Case 20).

Case 17. A nurse, aged 23, had erysipelas and was away for five weeks. She worked for three weeks with some tachycardia and then went to bed with a sore throat. Her temperature did not reach 100, but after a few days dropped beats were suspected clinically, and she was sent for a cardiogram which showed a P–R interval of 0·32 sec. Within three weeks it had fallen to 0·16 sec.

She has been under regular observation for ten years since and has never been off work or noticed any rheumatic or cardiac symptoms ; she may be a trifle short of breath, but no more than would be expected from her weight. There have been no physical signs in her heart, the P–R interval has remained at 0·16 sec., and neither before nor since have there been any symptoms suggestive of rheumatism.

Case 5. A girl, aged 18, was admitted for a sore throat, malaise, and a pain in the right shoulder that had been present for five weeks. Her temperature was 101, but became normal in three days and her general condition quickly improved. There were some doubtful signs at the right apex, but after X-ray and sputum examination tubercle was exluded, wrongly, as was found later. Her heart rate on admission was 85, but fell to about 44–56 during the first week and dropped beats were

diagnosed. On the tenth day the P–R interval was 0·29 sec., increased to 0·32 after exercise. She was not sent for a cardiogram again and was discharged apparently well after a few weeks. She was written for four months later, when she looked and felt well and the P–R interval was 0·21 sec.; but when written for again after two years she was found to be in hospital with bilateral tuberculosis and died soon after.

2. *Chronic heart disease.* There were thirteen in this group, excluding those where the dropped beats were caused by digitalis. On the whole they were older patients, mostly about 60. In this group, too, the dropped beats were generally transient. But in contrast with many of the younger patients, the underlying heart disease remained unchanged, and nearly always there was some permanent heart block ; sometimes this was only latent, but often it was 2 : 1 or a higher grade of block. Complete heart block and Stokes-Adams attacks were indeed not uncommon in this group. These points are dealt with more fully and the findings contrasted with those in the younger group, where the dropped beats were due to active infection, in the discussion that follows.

Discussion

Age incidence. Excluding the cases caused by digitalis where all ages and types of disease were found, there was a complete contrast between the two groups of those with active infection and those with chronic heart disease. The average age of the fourteen patients with infections was 32 years ; all were between 18 and 51, and all but three between 18 and 34. The thirteen without active infection were nearly all over 60. The average age of nine of them was as high as 67, and the average of all thirteen was only kept as low as 59, because of two patients, aged 22 and 42, with mitral disease, one, aged 49, probably syphilitic (Case 119), and one, aged 52, with rheumatic aortic incompetence. The patient, aged 22, was exceptional in many ways and the dropped beats may have been due to a recurrent infection if his lesion really was a rheumatic mitral stenosis, because during several years when he was under observation with latent heart block this was the only time he had dropped beats, and later treatment with digitalis seemed more liable to change the rhythm to auricular fibrillation than to dropped beats. There was no rheumatic history but a very persistent gonococcal prostatitis (Case 7).

The transient nature of dropped beats. In the patients of both these groups the dropped beats were very transient and generally lasted for some days only. Naturally this was so in the cases where they were caused by infections or digitalis treatment, though in Case 113 the partial block was unusual by lasting for as long as three months.

More unexpectedly, it was nearly as transient in the older cases. Many of these were seen regularly or intermittently for five or six or even for ten or twelve years ; and yet it was rare to have more than one or two plates with dropped beats unless these were taken about the same time. There was no patient with any reasonable expectation that dropped beats would be observed on any particular occasion he might be seen. The nearest approach to this was a doctor, aged 80, with mild anginal symptoms who said that he had noticed dropped beats, sometimes one in four, sometimes one in twenty, for about six years ; I expected to find extrasystoles, but as the P–R interval was 0·30 sec. on both occasions he was seen, I think that he was correct, though I was not lucky enough to record any dropped beats (Case 16).

Prognosis, especially as regards the persistence of block. In the younger group due to infections, the heart block was often as transient as the dropped beats, so that the P–R interval returned to normal and the patient made a very good recovery with a heart that was nearly if not quite as good as before. This was specially true of the cases with uncomplicated tonsillitis and often of those with acute rheumatism.

The nurse with dropped beats after tonsillitis may be quoted, as within a few weeks her heart was thought to be normal and her history during the subsequent ten years bears this out (Case 17, see p. 57). She was the patient whose heart could with the greatest certainty be called normal, though there were others who seemed to make a complete recovery ; several even of the rheumatic patients made a surprisingly good recovery, for example the young woman quoted with transient complete heart block who is still in good health twelve years later. The degree of recovery of the P–R intervals is well shown in Table II.

The only exceptions to this generally good outlook were the cases in which the infection was so severe that the patient died while still in the acute stage of his illness. The occurrence of heart block in cases where tonsillitis and hyperthyroidism were associated seemed of grave significance. There were three such patients, one having slight signs of hyperthyroidism and developing dropped beats after treatment with strophanthin when her septic tonsils had been removed (Case 28), one having a severe quinzy and slight evidence of hyperthyroidism (Case 23), and the other having exophthalmic goitre with partial heart block and dropped beats following an attack of tonsillitis (Case 25). The

last two were among the small number of patients who died soon after dropped beats were observed ; the former died with a patchy myocarditis, and the latter died at home and was said to have had a pulse rate of 20 before her death (she was not placed in the group with complete heart block as this only included proved cases).

By contrast the older group generally had a long P–R interval or a higher degree of block permanently, even though the dropped beats were only observed for a time. Furthermore, there was permanent heart disease as the underlying cause : e.g. high blood pressure and atherosclerosis (Case 3), an enormous heart and bundle branch block (Case 24), atherosclerosis and a P–R interval of 0·30 sec. in a man of 80 (Case 16), congestive failure after a probable coronary thrombosis (Case 6), and so on ; and as might be expected the prognosis are mainly dependent on this. Actually only five of the thirteen died while they were under observation, but unfortunately less care was taken to keep in regular touch with these older patients.

Another difference was that the younger group generally had no higher degree of heart block than the dropped beats, while this was quite common with the older group. Only three of the seventeen in the younger group had higher degrees of block : viz. the girl who had complete heart block followed by various grades of partial block during her acute rheumatism, and recovered without even latent heart block (Case 113) ; a woman of 45 with hyperthyroidism and tonsillitis who insisted on leaving hospital soon after her dropped beats had been recorded and died at home a few weeks later, probably with complete heart block (Case 25) ; and a man, aged 50, with congestive failure probably due to infective endocarditis, who had latent block, 2 : 1 block, and dropped beats within a few minutes on the same cardiogram (Case 109).

By contrast, rather more than half the older group with chronic heart disease had 2 : 1 heart block ; four of these were seen with complete heart block also, and one of them had a history of Stokes-Adams attacks. In addition, two of those, in whom neither 2 : 1 nor any higher degree of block was observed, gave a history (one certain and one doubtful) of Stokes-Adams attacks. A woman of 42 with rheumatic mitral disease may be taken as an example that the higher degree of block was the more usual finding in this group. Seen about twenty times in the course of five years, there was only one record with dropped beats, though latent block without dropped beats was seen several times in 1933 and in 1936 : most often there was 2 : 1 heart block, though sometimes this was changing to latent, and once there was complete block. Her symptoms had started with one Stokes-Adams attack and she died suddenly six years later, presumably in another such attack (Case 107). Or again an elderly woman with high blood pressure who had dropped beats the first time she was seen : subsequently until her death six months later she generally had complete but sometimes 2 : 1 heart block (Case 103).

In conclusion, partial heart block with dropped beats was very transient. In two thirds of the cases it was due to acute infections or to digitalis treatment ; rheumatic fever was the most common, and tonsillitis the next most common infection. When it was due to infection, the patients were nearly all young, between 20 and 34, and generally made a very good recovery. In one third there seemed no obvious precipitating cause of the dropped beats. These were older patients, generally over 60, with chronic heart disease that was often serious, and in half of them a higher degree of heart block such as 2 : 1 was the usual rhythm.

II. The Mechanism of Dropped Beats

In 30 of the 38 cases the diagnosis was made on electrocardiographic evidence, so that the P–R intervals could be measured; in the other 8, it was made by the clinical observation of dropped beats and a long P–R interval in the cardiogram. These will be considered in two groups—a small number with no progressive increase of the P–R interval and a larger number with progressive lengthening.

Dropped Beats with no Previous Lengthening

In 4 of the 30 cases the dropped beats occurred without any significant lengthening of the preceeding P–R interval. Lewis (1925, p. 177) states that this type of heart block due to " depression of excitability " was first described by Hay (1906) : his case showed 2 : 1 heart block with a normal a–c interval, and also the change from this to normal responses without any change in the a–c interval; there were no isolated dropped beats. This same type is, however, found in cases with dropped beats, the P–R interval being unchanged before and after the dropped beat, though generally prolonged.

The four cases of this type were an elderly woman with high blood pressure, who also showed 2 : 1 heart block, the P–R interval with all rhythms (latent and 2 : 1 block and dropped beats) being 0·21 sec. (Case 103): a man, aged 61, with high blood pressure, whose P–R interval was 0·25 sec.

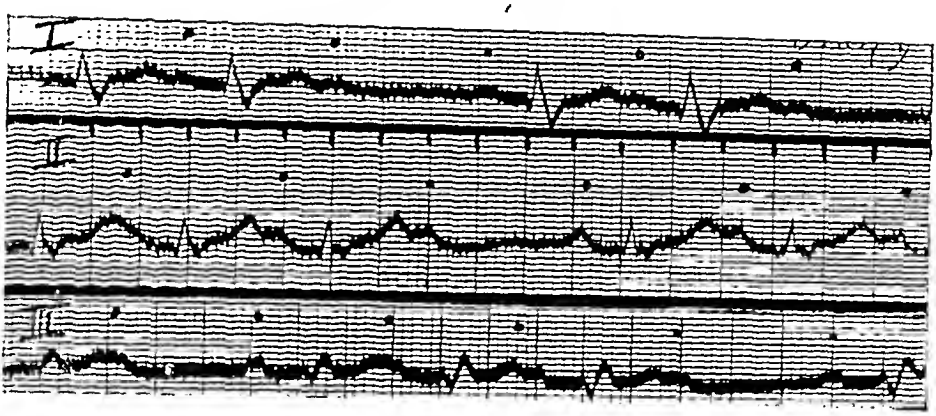

FIG. 1.—Fairly frequent dropped beats without any progressive lengthening of the P–R intervals which are all about 0·25 sec. John Hay's depression of excitability. From an elderly man with atherosclerosis and high blood pressure. Case 3.

In this and succeeding figures the auricular waves have been marked with dots (.), and the time-marker rulings have been inked to show up fifths of a second.

whether he had dropped beats or only latent heart block (Case 3, Fig. 1: a man, aged 66, with a large heart and bundle branch block; whose irregular heart was generally caused by extrasystoles and sino-auricular block, but sometimes by dropped beats after his extrasystoles, the previous P–R intervals remaining unchanged at about 0·24 sec. (Case 24); and a man, aged 30, with pericarditis and acute arthritis, where the position was less definite, the P–R interval often remaining constant at 0·48 for many beats before one was dropped, but shortening a little to 0·45 sec. afterwards (Case 21, Fig. 2). Another case, seen recently, was a woman of 80 whose P–R interval was 0·26 (and had

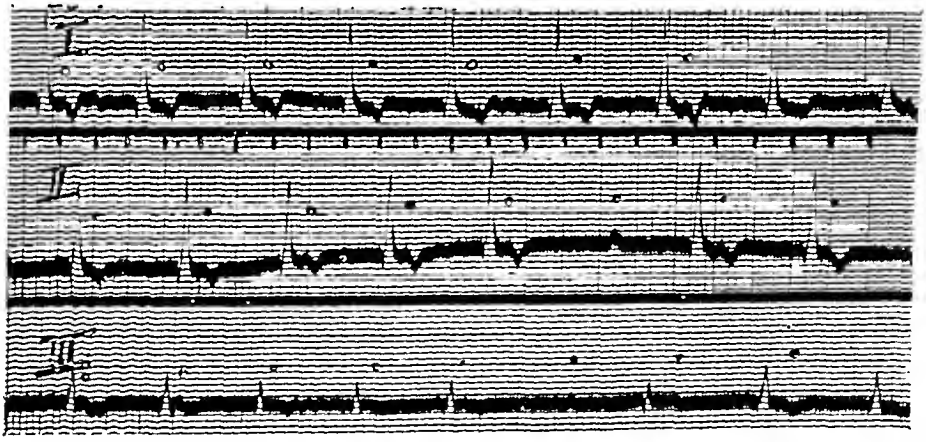

FIG. 2.—*Occasional dropped beats interrupting very long P–R intervals which are little changed.* Those before the dropped beat were all 0·48 sec. and the one after was 0·45 sec. From a young man with pericarditis and rheumatism. Case 21.

been the same six months before when she had no dropped beats); she had also wide QRS waves and almost the picture of bundle branch block. Four of these five patients were elderly and of the type where complete heart block would not be an unexpected finding.

Other cases suggested that changes and intermediate types between this group and the more usual one with progressive lengthening of the P–R intervals (Wenkebach's periods) are not uncommon, e.g. a man where four or five P–R intervals before the dropped beat had a constant length of 0·44, but one as short as to 0·28 sec. after the dropped beat (Case 14, Fig. 3). Another patient (Case 11), in whom the usual sequence of events was 0·24, 0·42 sec., d.b., etc., sometimes showed three or four final responses at a constant P–R of 0·42 sec. before the dropped beat.

Another with acute rheumatic carditis (Case 113), who showed all stages from one dropped beat after seven responses to 2: 1 heart block, gave a sequence that resembles this to some extent in that

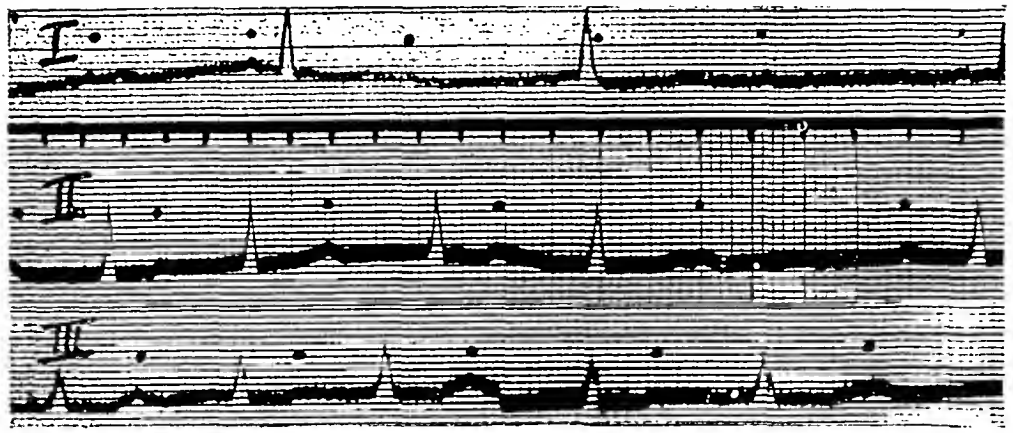

FIG. 3.—A dropped beat after a long series of unchanged P–R intervals, each being 0·44 sec., but with much shortening of the P–R interval (0·28 sec.) after the dropped beat. From a man with rheumatic aortic incompetence. Case 14.

the increase from 0·18 to 0·22 sec. during eight beats before a dropped beat seemed to remain steady in the middle period, e.g. 0·18, 0·20, 0·21, 0·21, 0·21, 0·21, 0·22, d.b. Inevitably as the number of responses before a dropped beat grows greater, the change in succeeding P–R intervals must be less, but one of the longest we have measured with a dropped beat after eight responses was: 0·28, 0·32, 0·32, 0·33, 0·34, 0·37, 0·39, 0·40, d.b. (Case 10).

A young woman in whom dropped beats were only noted after vagal pressure in the neck (Case 23) may throw some light on the mechanism involved. Though at times her response was 0·20, 0·40, d.b., etc., at other times it might be: 0·32 (6 times), 0·36, d.b.; or 0·20, 0·29, 0·34 (4 times); possibly because the effective pressure on the vagus was not sufficient to produce the first more usual response.

DROPPED BEATS WITH PROGRESSIVE LENGTHENING

Omitting the 4 cases that gave dropped beats with no previous lengthening, there were 26 left to study the rate of lengthening of the P–R interval before the dropped beat. In some of these, various responses (e.g. 3 : 2, 4 : 3, 5 : 4, etc.) were observed (Cases 2 and 113 gave the most complete series for comparison in a single case); in others the responses were all of the same type. Naturally 3 : 2 heart block was seen most often (18 cases) and then 4 : 3 block (9 cases).

3 : 2 *Heart block.* This was observed in 18 cases; in a few there was only a single record, but in the great majority there were at least three or four measurements, which would help to eliminate chance errors.

There were great variations in the length of the P–R intervals in different patients, without any obvious relationship to the degree of heart block or to the type of diseased heart. Thus, the first P–R interval after the dropped beat might be a little below 0·20 sec. or as long as 0·30; the last before the dropped beat might be as short as 0·25 or as long as 0·40; and the difference between the two P–R intervals might be as much as 0·20 or as little as 0·10 or sometimes even 0·05 sec. These figures are given more accurately in Table IV; they were very much the same in the different grades of heart block. It was rather surprising to find this, as one might expect that where the first P–R interval was 0·28, a dropped beat would be likely to occur sooner (i.e. after fewer responses) than in a case where it was only 0·20 sec.; and that the difference between the first and last P–R interval would be

TABLE IV

VARIATION IN FIRST AND LAST P–R INTERVAL AFTER AND BEFORE A DROPPED BEAT

Grade of heart block	First P–R	Last P–R	Difference between first and last P–R
3 : 2	0·18 to 0·29	0·26 to 0·42	0·046 to 0·20
4 : 3	0·18 to 0·29	0·25 to 0·41	0·07 to 0·17
5 : 4	0·17 to 0·29	0·27 to 0·43	0·045 to 0·21
6 : 5	0·19 to 0·28	0·26 to 0·43	0·07 to 0·16
7 : 6	0·18 to 0·28	0·23 to 0·44	0·045 to 0·22

much greater where there were six responses before a dropped beat than when there were only two. It suggests, as do other findings, that more than a depression of conductivity is concerned in the production of dropped beats.

It was quite common for the P–R interval to lengthen to 0·40 or even 0·44 sec., as will be seen from figures of this magnitude occurring in each grade of heart block in Table IV. Exceptionally, however, as in a man who died with tuberculosis of the lungs and nephritis, it lengthened more than this, from 0·29 to 0·56 sec.; later as his general condition became worse the heart rate quickened to 100, but no further cardiogram was obtained (Case 20, Fig. 4).

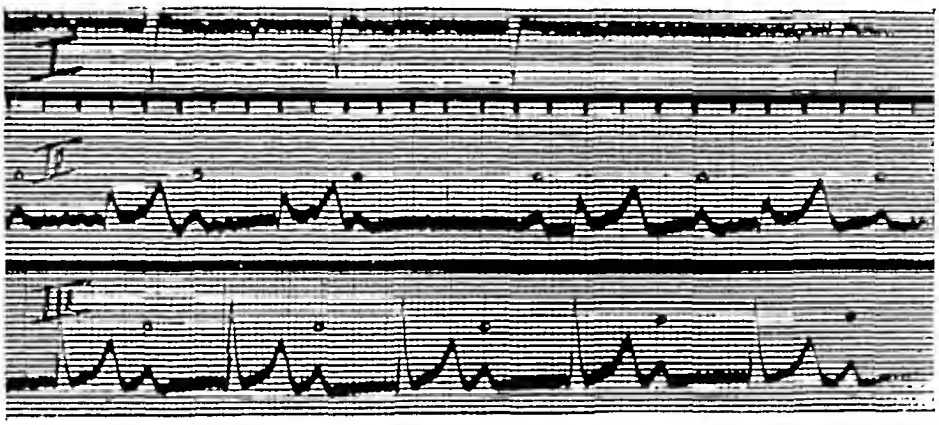

FIG. 4.—Unusually long P–R intervals, 0·56 sec., sometimes very regular as in lead III, sometimes shortening considerably to 0·29 sec., after a dropped beat as in lead II. From a man with tuberculosis, nephritis, and dextrocardia. Case 20.

I have not been able to find that any type of patient or type of heart disease is specially prone to fall into the groups with the longer or shorter P–R intervals. Taking the cases of any one grade of heart block there was some slight tendency for a short first P–R interval to be followed by a relatively short last P–R; e.g. if the cases were averaged in three groups according to the length of the first P–R interval the sequences were 0·19, 0·32, d.b.; 0·22, 0·35, d.b.; and 0·25, 0·36, d.b. But there was no close correspondence and there were many exceptions.

The average figure for the whole series (allowing a little extra weight to the cases where there were many records) was 0·227, 0·347, d.b., etc., but an arithmetical average without any weighting would have made little difference as this would have given the sequence 0·232, 0·345, d.b., etc.; subsequent figures were therefore obtained by the arithmetical average.

4 : 3 *Heart Block.* This was observed in nine cases and in most of them there were several measurements. There was again great variation in the first and last P–R intervals and in the difference between them, these covering about as wide a range as with 3 : 2 heart block. Lewis (1925, p. 177) states: "It is the rule for the dropped beat to be foreshadowed by progressive lengthening of the P–R interval. The increase of the second interval over the first is greater than the increase of the third over the second, or more generally: as the P–R interval increases the rate of increase in the P–R interval diminishes and the ventricular rate consequently quickens slightly." Six of the nine cases agreed with this, giving an average sequence P–R, 0·236, 0·304, 0·341, d.b., etc., the increment being 68 and 37, but in many of them the difference was not great. One (Case 13) showed this in an extreme form (Fig. 5) the sequence being 0·24, 0·37, 0·41, d.b., etc. In the seventh the intervals were equal and in the eighth the sequence was 0·18, 0·21, 0·25, d.b. The ninth (Case 2) showed the reverse relationship, the sequence being 0·25, 0·31, 0·39, d.b. The average figure for all nine cases was 0·238, 0·297, 0·340 sec., d.b., the first increment being greater than the second in the porportion of 59 to 43.

5 : 4 *Heart Block.* There were five cases, all but one with two or more records that could be measured. There was the same variation in the first and the last P–R intervals (see Table IV). The average figures were 0·239, 0·281, 0·314, 0·349, d.b., etc., and again the difference between the first two was the greatest but not to any very marked extent, the figures being 42, 33, 35. Taking the individual figures they were more evenly spaced than in the other groups, but probably this was no more than chance. It was, however, significant that nearly all the cases in this group and the groups with higher grades of heart block were due to digitalis treatment or to acute infections.

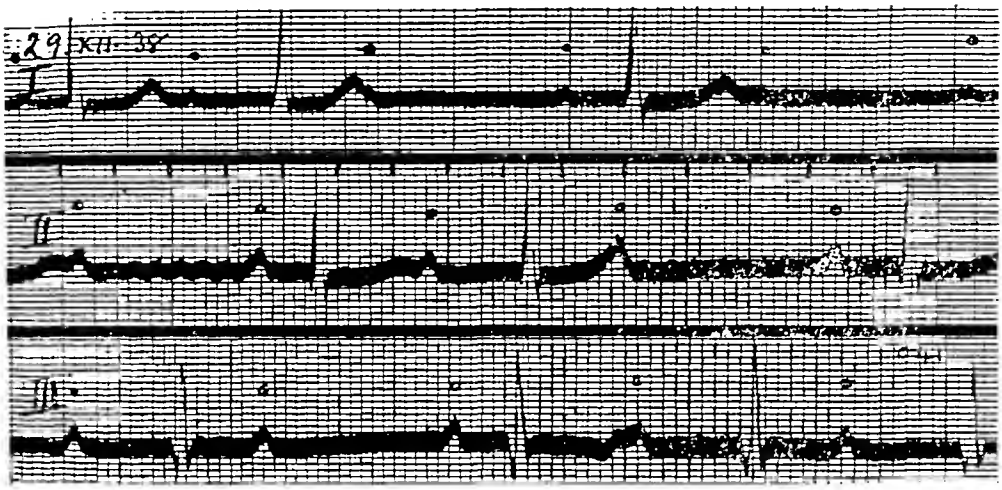

FIG. 5.—Generally 3 : 2 heart block (P–R, 0·25, 0·37, d.b., etc.), but at the end of lead III, 4: 3 heart block with Wenckebach's periods: P–R, 0·24, 0·37, 0·41 sec., d.b., etc. The amount by which the first increment exceeds the second is here exceptionally large, though it is usual for the first increment to be larger than the second or subsequent ones. From a young man with rheumatic fever. Case 13.

6 : 5 and 7 : 6 *Heart Block.* Naturally there were fewer examples of these types and much stress cannot be laid on the average figures as they were only based on four and three cases respectively. There was much the same range in the first and last P–R intervals and in the difference between them as in the higher grades of heart block discussed. The average sequence of P–R intervals is shown in Fig. 6 and in Table V with the averages of the other groups. In both these groups the increment

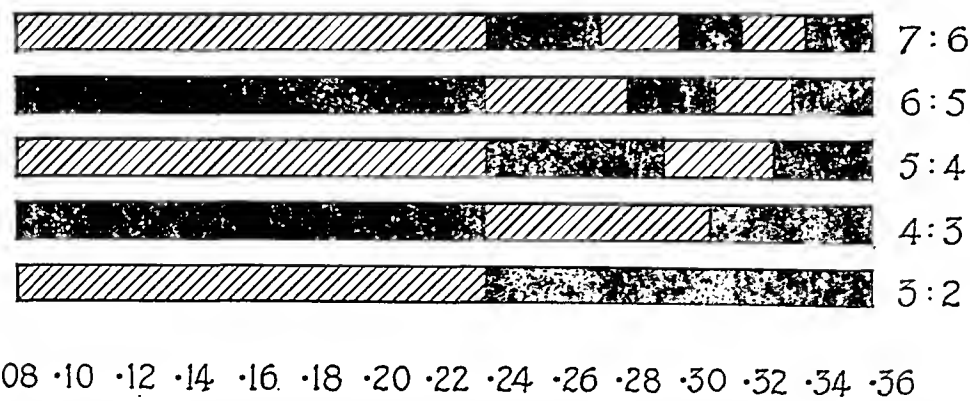

FIG. 6. Diagram showing the length of the successive P–R intervals with different grades of heart block. Drawn from the smoothed figures given in Table VI.

was greatest between the first and second intervals, but after that the increment seemed to be fairly regular, the figures being 37, 22, 21, 25 (6 : 5); and 41, 22, 21, 20, 23 (7 : 6). In the last three groups there seemed a slight tendency for the last increment to be a little higher than any of the other figures except the first; in some individual cases it seemed to be more noticeable but rather inconstant.

DISCUSSION

The average figures for the P–R intervals with different grades of heart block with dropped beats (d.b.) are shown below in thousandths of a second :

TABLE V

3 : 2 heart block	227, 347, dropped beat.
4 : 3 ,, ,,	238, 297, 340, d.b.
5 : 4 ,, ,,	239, 281, 314, 349, d.b.
6 : 5 ,, ,,	232, 269, 287, 308, 333, d.b.
7 : 6 ,, ,,	226, 267, 289, 310, 330, 353, d.b.

Wenkebach (1904) discussed this gradual lengthening of the a–c interval in his book on arrhythmia of the heart; he says " the interval is shortest at the first contraction after the pause, it is considerably longer at the second, and increases only a little more in length with succeeding systoles." He spoke of Luciani's periods and also described similar results obtained by Englemann in experiments with cardiac muscle; from this he deduced that it was due to a fundamental property of cardiac muscle and not to some special property of the fibres forming the block at the A-V groove.

Of two series of figures he quoted, chosen at random, 0·235, 0·30, 0·322, 0·345, 0·365, d.b.; and 0·23, 0·37, 0·40, 0·43, 0·45 sec., d.b.; the former is near to the average found in this series and the latter is an instance where the first increment exceeds the other increments by much more than usual. Basing his arguments on his own work (*Über den regelmässig intermittierenden Puls*, 1899), and especially on that of Mackenzie, he argued that clinical heart block is a defect of conductivity. Partly as a result of his work, this is now so widely recognized that the difficulty of accepting it as the whole explanation is sometimes forgotten—a point which will be discussed later.

To return to the figures obtained in this series: the first P–R interval averaged 0·232 sec. and the last 0·345 sec. As some were above and some below this without any regular graduation, one can get a better comparison of the intermediate figures by adjusting all the first figures to 230 and all the last to 350 with corresponding adjustments of the other figures. There will still be irregularities due to errors and the small sampling, but by plotting out the figures and drawing smoothed curves one gets a more regular series of figures which are probably a better approximation to the truth; these are shown below.

TABLE VI.

3 : 2 heart block	230, 350, dropped beat.
4 : 3 ,, ,,	230, 300, 350, d.b.
5 : 4 ,, ,,	230, 286, 319, 350, d.b.
6 : 5 ,, ,,	230, 275, 303, 327, 350, d.b.
7 : 6 ,, ,,	230, 266, 292, 312, 332, 350, d.b.

The first group of figures were submitted to Professor W. A. H. Rushton of Cambridge with the request for a mathematical formula covering their relationship. He very kindly considered the problem and wrote that the following formula has no arbitrary constants, is easy to compute, and seems to fit on the whole pretty well. If the grade of heart block is N+1 : N, the P–R interval for the nth beat after a dropped beat is given by T in thousandths of a second, where

$$T=250+120\frac{n-1}{N}-\frac{20}{10^{n-1}}$$

The corresponding figures calculated from this formula agree fairly well with the observed figures, except in the case of the second beat with 3 : 2 heart block where the calculated figure is much smaller; they are :

TABLE VII

3 : 2 heart block	230, 308, (370)
4 : 3 ,, ,,	230, 288, 330, (370)
5 : 4 ,, ,,	230, 278, 310, 340, (370)
6 : 5 ,, ,,	230, 372, 298, 322, 346, (370)
7 : 6 ,, ,,	230, 268, 290, 310, 330, 350, (370)

It thus appears from Professor Rushton's figures the beat is dropped when the P–R interval would have become as long as 0·37 sec. Looking at the same problem in a slightly different way I had concluded that there was a response when the P–R interval was 0·35 sec., but not when it reached a longer time than this. One must remember that these are *average* figures and that in individual cases they may be a good deal higher or lower.

In 15 cases it was possible to make a comparison between the P–R interval at the times when there were and when there were not dropped beats. With the dropped beats, the average P–R interval increased from 0·26 sec. to 0·37 sec.: without the dropped beats, it was 0·30 sec., an intermediate figure nearer to the P–R interval of the first response after the dropped beat. Actually, in 7 cases it was the same as the P–R interval of the first response, and only in 3 cases was it the same as the P–R interval of the last response before the dropped beat.

In 9 cases (Table III) one could also compare the P–R interval with 2 : 1 heart block. The average figures were : first response after the dropped beat, 0·24; last response before a dropped beat, 0·34; latent heart block with no dropped beats, 0·27; and 2 : 1 heart block, 0·25 sec.

It is interesting that the P–R interval with latent heart block with no dropped beats, the P–R interval of the first response after a dropped beat, and the P–R interval with 2 : 1 heart block should all be so close—0·24 to 0·27 sec. in these cases.

The correspondence of these three, both in average and in individual figures, and our observations that whatever the grade of heart block—whether there are dropped beats after two responses or after six or seven—the first P–R interval after the dropped beat averages 0·23 sec. and the last before the next dropped beat 0·35 sec. must be taken into account in any explanation of heart block.

The real difficulty has always been to explain why in one case a P–R interval of 0·35 sec. gets no longer and is regularly followed by a response, and yet in another case a P–R interval that is shorter or nearly normal lengthens till it reaches a stage where a beat is dropped.

If the higher grades of heart block were always associated with the very long P–R intervals such as 0·35–0·40 sec., and the lower grades with shorter P–R intervals such as 0·25–0·30 sec., one could look on the defect of conductivity as the whole or almost the whole explanation. But when it is possible to have a P–R interval of, say, 0·24 sec., with regular responses and no dropped beats or a P–R interval of the same duration with dropped beats or with 2 : 1 block, a second factor must also be involved.

It seems that depression of excitability, the main explanation in the cases described by Hay, is also concerned in all these other cases. The separation of the function of cardiac muscle into its four divisions, of which conductivity and excitability are two, has been criticized, but clinical study of heart block suggests that these two at any rate are both involved in the production of most cases of heart block. Probably the same factors that affect conductivity also affect excitability of the ventricle, and the grade of heart block depends on the interaction of these two.

Summary and Conclusions

Partial heart block with dropped beats is nearly always transient, so that it is rare to find a patient in whom this rhythm can be expected as a usual or even as a common finding.

At one time or another it was observed in nearly one sixth of a series that included all types of heart block, but this gives an exaggerated idea of its frequency because it was generally transient and of short duration.

In two thirds of the cases (25 out of 38) there was a known cause, active infection or treatment with digitalis. In 14 the cause was an acute infection, in 5 it was treatment with digitalis, and in 6 both causes combined. As would be expected, acute rheumatism was the most common infection (9 of 20 cases) ; but tonsillitis, without any suggestion that it was rheumatic, was often found.

The patients with dropped beats due to infections were mostly between 18 and 34 years of age. The outlook in this group was surprisingly good and the patient often recovered even to the stage of a normal P–R interval. As an exception the simultaneous association of tonsillitis and hyperthyroidism with dropped beats seemed of grave significance.

In the remaining third (13 cases) there was chronic heart disease and no very obvious reason why the dropped beats should have been found at the time they were, for here, too, they were generally transient. These were older patients, nearly all well over 60 years of age: all had chronic heart disease; high blood pressure and coronary atheroma were each the ætiological factor in one third, and in the remaining third there was myocardial disease without evidence of either of these factors.

In addition, some degree of heart block generally remained in the group of older patients, half of them having 2 : 1 heart block as a common or as their most usual rhythm. This was not so with the younger patients. Complete heart block also was uncommon in the group of younger patients with infections, but was present at some time in about one quarter of the older group. The regular sequence of dropped beats, 2 : 1 heart block, and finally complete heart block was observed, but was rare.

The length of the P–R intervals was also studied. Progressive lengthening, but with a decreasing increment, was the rule, the increase of the second P–R interval over the first being much larger than the subsequent increases. There were, however, exceptions. In about one eighth of the cases with dropped beats, these came without any gradual lengthening of the P–R interval (Hay's depression of excitability); these patients were mostly older ones with chronic heart disease.

For each grade of heart block up to a dropped beat after six responses, there were enough records to give some average figures, which have been shown in Table V and Fig. 6 and can be given more shortly as

3 : 2 heart block ; 0·23, 0·35 sec., dropped beat.
4 : 3 „ „ 0·23, 0·30, 0·35, d.b.
5 : 4 „ „ 0·23, 0·285, 0·32, 0·35, d.b.

It must, however, be repeated that these are only the average of figures that varied widely in the different cases. It is strange that the average and the range of the P–R intervals between the first response after and the last response before the dropped beat should be so constant, whether there is one dropped beat to 3, 4, 5, or 6 responses. This finding and some of the other points that have been discussed suggest that the defect of conductivity is generally the condition which makes heart block likely, but that something else, probably excitability, decides if there will be block and, if so, of what grade it will be.

I should like to express my thanks to my colleagues at Guy's Hospital and at the National Hospital for Diseases of the Heart for allowing me to continue observations on some patients who were under their care. Without the help of Dr. S. Suzman as Clinical Assistant and Mr. F. H. Muir as technician, it would not have been possible to keep in touch with so many patients or to get so much information about patients who were generally first seen during busy routine sessions. Such work has obvious limitations and in some directions more could have been found out in a few days by intensive experimental observations on one patient. Nevertheless, the less complete study of a series of unselected cases gives other information that can only be obtained in this way and the two methods are complimentary. The loss of my longer paper-camera records of many of these patients as a result of enemy action has limited the study to shorter plate records.

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THE REFERENCE OF CARDIAC PAIN TO A PHANTOM LEFT ARM

BY

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Two cases in which anginal pain was referred in part to a " phantom " left arm are here recorded as a contribution to the problem of the mechanism of referred pain. In both, (1) the left arm had been amputated more than 25 years before the onset of cardiac pain, (2) there was evidence, both clinical and cardiographic, of gross myocardial damage, and (3) the " phantom " component of the pain was abolished, or significantly modified, by anæsthetizing the left brachial plexus.

Case I. Cardiac infarction; left bundle branch block. Phantom left arm since 1916 *following amputation through upper arm; cardiac pain referred to phantom and chest (April,* 1942). *Left brachial plexus block eliminated " phantom " component.*

H. T. (admitted 26/5/42), male, aged 45 years, in charge of social department of Tramways Depôt for 16 years; married; childless; wife healthy. Smokes 10 to 15 cigarettes daily but life-long teetotaler. No history of illness before 1916, and except for occasional colds and winter cough excellent health since discharge from the army. No significant family history of cardiovascular sclerosis.

On October 8, 1916, in France, he was wounded above the left elbow; ten days later the arm was amputated because of gangrene. Progress was good though three months later, owing to a persistent slight discharge, he had another operation. The wound then healed rapidly and completely. From the time of the amputation he has had a phantom arm, at first equal in length to his right arm, though gradually it has shortened to about half its original length; it moves with the shoulder but the elbow, forearm and hand remain fixed—the elbow at about 90° flexion, the forearm in mid-pronation-supination, and hand and finger joints slightly flexed—" as if clutching a ball." The hand dominates the phantom and he can discern all fingers clearly. The awareness of the phantom is not due to pain but to a tingling which he is usually able to ignore; "you get quite used to its being there." Wet weather intensifies the tingling.

FIG. 1.—Case 1. Showing the amputation stump and scar.

On April 6, 1942, an hour after rising, he was seized suddenly with pain in the substernal and left submammary region which spread to the stump and radiated down the phantom to the fingers, though the worst pain was felt in the phantom biceps region. Waterbrash and one small vomit accompanied this attack, which passed off completely in less than an hour; he went to his work that day and experienced no further pain, breathlessness, or other chest symptoms. During the following six days he had occasional twinges of the pain, but on April 12, whilst in bed, he had an attack similar in type, intensity, and duration to that of April 6. Since then the pain has recurred on undue effort, though the effort needed to produce pain radiating to the phantom varies; rest for a minute or two invariably eases the pain, which is induced by less effort in the morning than in the afternoon.

Examination showed a stump, four inches long (Fig. 1), with free and full movement at the shoulder joint and slight hyperæsthesia of the scar.

The heart was slightly enlarged and Dr. Roberts reported: Slight enlargement of left ventricle;

no evidence of pathological calcification, or of pulmonary lesion. The sounds were normal, the rhythm regular, and there was no murmur. B.P. 110/60. Pulse rate 78. Early locomotor brachial artery and slight retinal arteriosclerosis. There was typical left bundle branch block (Fig. 4A).

There were no significant clinical changes in the lungs, nervous system, or abdomen; no evidence of sepsis in mouth (edentulous) or naso-pharynx, and no pyrexia during his stay in hospital; no thyroid change, no skin rash, nor palpable lymph nodes. The urine was normal except for a few squamous cells and leucocytes with large numbers of calcium oxalate crystals. A blood count was also normal. The Wassermann reaction was negative.

On June 5, 1942, Mr. Edwards blocked the left brachial plexus with 60 c.c. of 1 per cent solution of procaine and Fig. 2 shows the extent of the resulting anæsthesia. No ocular or vascular changes

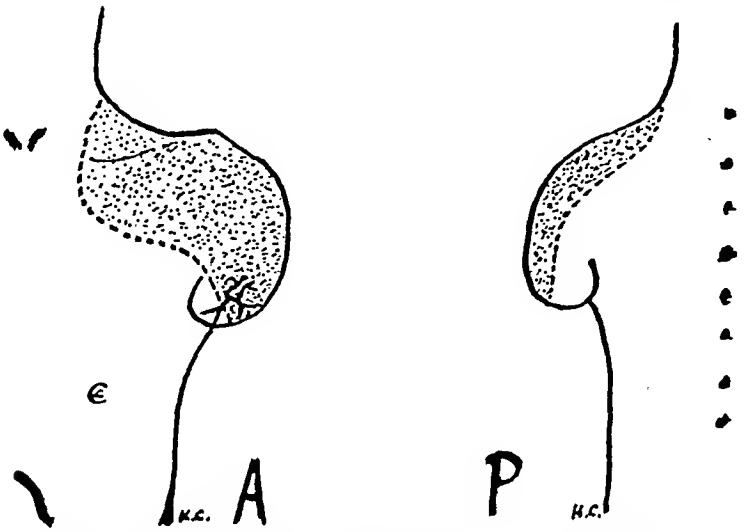

FIG. 2.—Case 1. The dotted area maps the anæsthesia resulting from the brachial plexus block. A. Anterior view. P. Posterior view.

were seen. The lower part of the scar remained sensitive though the patient felt that the whole phantom was numbed. Ten minutes later he walked 400 yards briskly; pain was felt in the chest only; the arm was quite free from pain though he had never previously experienced pain in the chest without radiation to the arm. When the anæsthesia passed off, exercise brought on pain in both chest and arm.

The variability in the intensity of effort required to produce the pain prevented quantitive observations on this patient. It is, however, of interest to note that since the brachial plexus block the phantom has shortened; he is no longer aware of arm or forearm, the hand appearing to be attached directly to the stump, and exertion now causes pain to appear in the chest and hand and/or stump simultaneously.

Case II. Angina of effort; coronary arteriosclerosis. Phantom left forelimb since 1916 following disarticulation through shoulder joint; cardiac pain present and gradually intensifying for 5 weeks; referred to phantom, neck, jaws, and chest. Left brachial plexus block practically eliminated phantom component, and modified sequence of appearance of pain in different sites.

J. T. (admitted 26/5/42), male, aged 51 years, a credit draper with no strenuous work; single; smokes 25 to 30 cigarettes daily and drinks an occasional beer. Father died at 52 from angina pectoris, mother at 74 from cerebral hæmorrhage, 5 sibs alive and well, a sister died aged 9 of spinal caries.

On August 9, 1916, his left humerus was shattered by machine-gun fire. He was treated at a field dressing station, but two days later, because of gangrene, the arm was disarticulated through the shoulder joint. A painful phantom appeared immediately, confined to the left hand, which was somewhat nearer to the shoulder than the right hand, and hanging at his side with fist clenched and nails digging into the palm, though the individual fingers were not distinguishable. The hand felt constantly swollen and burning, worse by night, and there were sharp stabbing pains on excitement. No voluntary movement of the hand or fingers was possible, but during the first two months he noticed that when he gripped with his right hand the phantom hand seemed to clench more tightly.

In 1917, an attack of acute appendicitis with operation caused an exacerbation of pain which subsided in a month. During the next 10 years, there was no change in the shape, site, or posture of the phantom, but the pain in it increased. In 1927, neuromata were excised from the scar; this operation improved the pain, caused the phantom to rotate inwards, and increased the appreciation of its site; but its shape and length relative to the shoulder remained unchanged at first, though very gradually during the next 15 years the limb shortened till now the phantom hand corresponds in site to the normal elbow. During the day the phantom was practically unobtrusive, though he could recall it by " thinking about it "; when he was tired, e.g. at the end of a day's work, the hot, swollen phantom reappeared. Thundery and wet weather always intensified the pain.

Five weeks before admission, after walking 300 yards up a steep incline, he noticed pain in his left shoulder and in the phantom hand " as though it had been battered to pulp "; this was followed when effort was continued by suffocation, constriction of the chest, pains in neck and jaws, and he felt " as though he would have died had he kept on walking." He rested and the pain eased. Since then, however, pain has recurred with gradually lessening exertion, until now walking 150 yards on the flat will bring on in unvarying sequence pain in the phantom, then in the neck, then a sense of constriction in the chest and choking. In the past fortnight there has been increasing breathlessness; now the act of undressing at bedtime leaves him breathless and exhausted and brings on the pain. He has had no cough, sputum, or other chest symptoms; no indigestion; no bladder disturbance; and no loss of weight.

Examination showed the scars of the disarticulation extending from the left acromio-clavicular

A B

FIG. 3.—Case 2. (A) Showing site of the amputation through the shoulder joint. (B) The scar is inked in and a pin-head neuroma indicated at X.

joint to the fifth rib in the mid-axillary line (Fig. 3); it was tender at X (Fig. 3B); pressure on this spot gave rise to a bursting sensation in the phantom similar to that experienced on exertion.

The heart was slightly enlarged and the X-ray report was: Slight enlargement of the left ventricle; bilateral simple fibrosis of the lungs. The sounds were normal, the rhythm regular and there was no murmur. B.P. 120 70. Pulse rate 84. Early locomotor brachial artery with slight silver wire thickening of retinal arteries. A cardiogram (Fig. 4B) showed low voltage and negative T_2 and T_3 waves.

He had slight emphysema, and an early arcus senilis. There was no organic lesion in the nervous system; no evidence of sepsis in mouth (edentulous), or naso-pharynx; no abdominal abnormality except the appendix scar which was well healed; no thyroid change; no rash; no palpable lymph nodes.

The urine was normal. The blood showed no anæmia. The Wassermann reaction was negative.

On June 5, 1942, Mr. Edwards blocked the left brachial plexus with 60 c.c. of 1 per cent solution of procaine. The diagram of the resulting anæsthesia (Fig. 5) shows that the lower part of the scar escaped, due to its dorsal nerve supply. On anæsthetization, the phantom lengthened and felt "like the gum when the dentist injects a local anæsthetic." No ocular or vascular changes were seen. About 20 minutes later he walked briskly on the flat (at a rate of 96 paces of two feet a minute): after 200 yards the suffocation and pain in the neck appeared but there was no pain in the hand; as he continued to walk he became conscious of the presence of the phantom and could discern the middle finger as a separate structure; and finally, when pain in the chest was so severe that he had to stop (after 600 yards), he was beginning to feel a mild bursting sensation in the phantom hand.

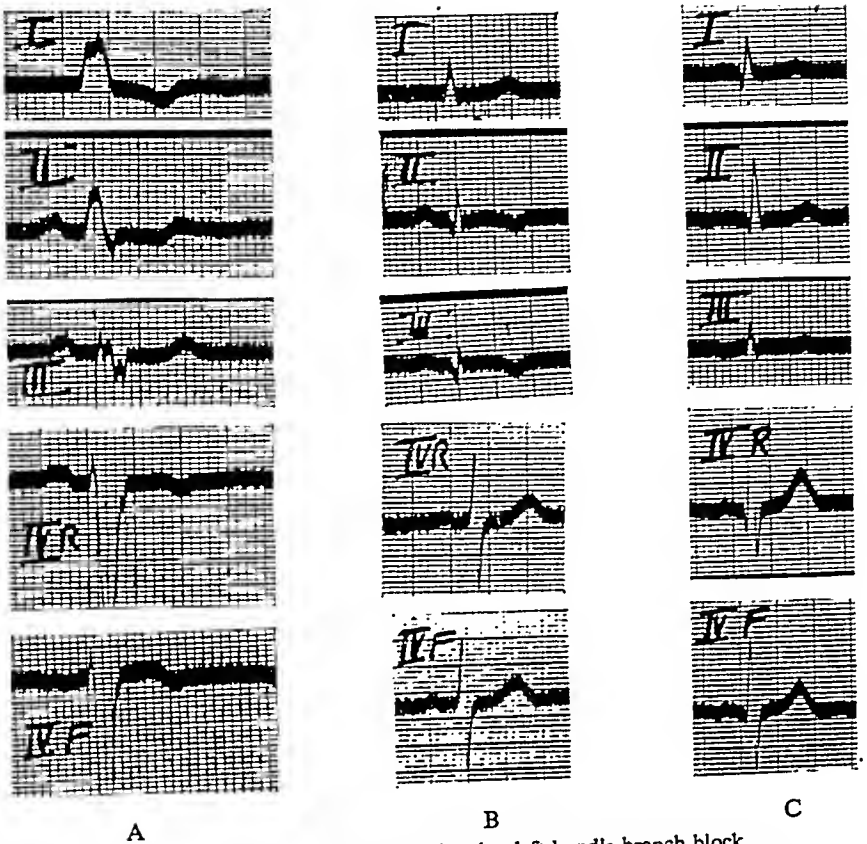

FIG. 4.—(A). Case I. Cardiogram showing left bundle branch block.
(B) Case 2. Cardiogram showing low voltage and negative T in leads II and III.
(C) Cardiogram from control patient with left upper phantom but no cardiac pain.

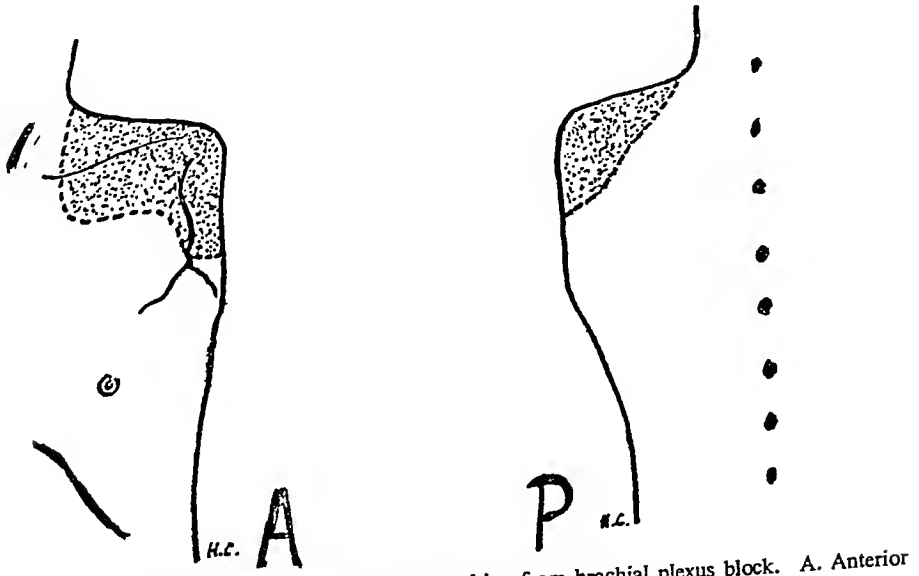

FIG. 5.—Case 2. The dotted area maps the anæsthesia resulting from brachial plexus block. A. Anterior view. P. Posterior view.

When the effects of the anæsthetic passed, the sequence of the angina reverted to phantom first (which appeared after about 150 yards walking on the level at a rate of 96 paces of 2 feet a minute), followed by suffocation, chest constriction, and neck pain (after 200–250 yards). A week later normal saline was injected into the plexus; this did not modify in any way the distribution of the pain, the order of appearance of its components, or the intensity of effort needed to induce it.

On July 20, 4 c.c. of 2 per cent novocaine was injected into the region of the neuroma at X (Fig. 3B). The effect on the cardiac pain was similar in type to that following the plexus anæsthesia. After walking 220 yards, constriction of the chest and choking appeared; as he continued this became very severe and then he felt the bursting pain in the phantom hand.

Comments

Fig. 4 C was taken from a patient with a phantom left arm who was otherwise quite well. It shows that fixing the left arm electrode to the amputation stump in no way modifies the cardiogram.

Great care was taken to avoid infiltrating the stellate ganglion when injecting the brachial plexus, as it is known that angina can be relieved by blocking the afferent impulses arising from the heart and passing through this ganglion. Apart from the visible evidence of the extent of the plexus infiltration two facts showed that the stellate ganglion had not been anæsthetized: first, the absence of any ocular or vascular signs of sympathetic paralysis; and secondly, the persistence of anginal pain in the areas not rendered anæsthetic by the brachial plexus block; had the stellate ganglion been blocked *all* afferent impulses from the heart would have been prevented from reaching the sensorium.

A careful search of the available journals has failed to reveal any comparable record of a patient who referred anginal pain to a "phantom." It is proposed in a later paper to discuss the bearing of our cases and the results of brachial plexus and neuroma block on current theories of referred visceral pain. It will be patent, however, that no such theory is tenable which fails to account for (i) reference of the pain to a phantom, and (ii) the effects of brachial plexus and neuroma block.

Summary

Two cases are recorded of cardiac pain referred to a phantom left arm.

Anæsthetization of the brachial plexus of the phantom caused, in one case, abolition of the phantom component of the cardiac pain, and in the other significant delay in the appearance of the phantom component which led to a reversal of the site of onset and spread of the cardiac pain.

CHEST LEAD CR_7 IN CARDIAC INFARCTION

BY

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From the Cardiac Department of the London Hospital

Received December 30, 1942

The value of limb leads in the localization of early cardiac infarction is known, and there is general agreement that the T I type of electrocardiogram indicates anterior infarction, and the T III type, posterior infarction (Parkinson and Bedford, 1928; Wilson, Hill, and Johnston, 1934, 1935, & 1938). The recognition of the lesion at a later stage, however, has sometimes proved difficult although changes in the chest lead IVR sometimes confirm the presence of an anterior infarct when the limb leads are doubtful. No such help is yet available in posterior infarction, and the frequency with which T III is inverted in healthy subjects complicates the problem in diagnosis if the history and clinical findings are equivocal. We have, therefore, sought a chest lead that would implement the limb lead cardiogram in the diagnosis of posterior cardiac infarction. During our investigation, Nyboer (1941) published his paper describing an abnormal œsophageal cardiogram in cases of healed posterior infarction. Using the œsophageal electrode at the level of the ventricle the T wave was often inverted. We confirmed this observation in several patients, but the discomfort caused by the test obviously detracts from its routine use. After testing several new chest leads we obtained the best results from one in which an electrode placed in the left posterior axillary line at the level of the inferior angle of the scapula was paired with one on the right arm. We suggest that this lead should be known as CR_7. This terminology is in keeping with the recommendations of the American Heart Association (1938) which applied the prefix C to all chest leads, and CR to those paired with the right arm; the chest stations were numbered 1 to 6 from right to left starting in the fourth intercostal space immediately beyond the right sternal border and ending in the left mid-axillary line. It follows naturally that the chest station in the posterior axillary line should bear the designation CR_7. An exploring electrode in this region was used by Wood *et al.* (1933) in their lead VI, but it was paired with one on the left leg and is not comparable with our CR_7.

We recorded the CR_7 cardiogram in 18 healthy subjects, in 32 patients with posterior cardiac infarction, in 12 with anterior infarction, and in 52 with some other form of heart disease. The changes observed in these four groups will now be described and compared with changes in the limb lead cardiogram, which was always a preliminary test.

CR_7 IN HEALTHY SUBJECTS

There were 18 cases whose clinical history and examination, which included cardioscopy, showed that they were healthy. They were chosen for the investigation because T III in their limb lead cardiogram was found to be inverted. Often this deformed T III was corrected by change of posture or respiration, but such effects do not concern us here. T I was always upright. In 13, T II was also upright, but in 4 it was low and in 1 it was flat. The T wave in CR_7 was invariably upright (Fig. 1).

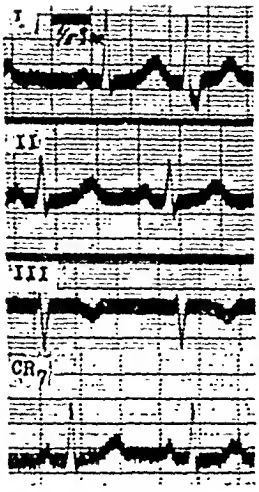

FIG. 1.

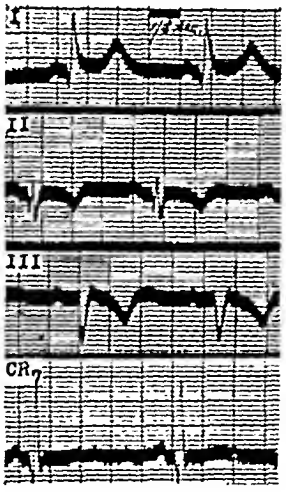

FIG. 2.

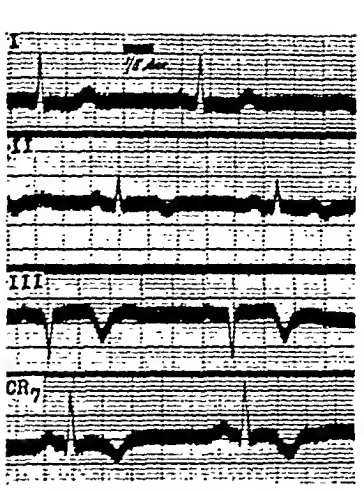

FIG. 3.

FIG. 1.—Healthy subject, aged 22. T inverted in III and upright in CR_7.

FIG. 2.—Posterior cardiac infarction of four years' duration. Male, aged 68. T inverted in II and III, and low in CR_7. R–T segment raised in I.

FIG. 3.—Recent posterior cardiac infarction. Female, aged 54. T II and T III inverted. Inversion of T in CR_7 greater than in II.

TABLE I

T WAVE IN CR_7 COMPARED WITH T II AND T III IN POSTERIOR CARDIAC INFARCTION

Case No.	State of T wave in limb and chest leads			Change greater in T II or in T CR_7
	III	II	CR_7	
1	Inverted	Inverted	Upright	T II
2	,,	,,	Low	,,
3	,,	,,	,,	,,
4	,,	,,	,,	,,
5	,,	,,	,,	,,
6	,,	,,	,,	,,
7	,,	,,	,,	,,
8	,,	,,	,,	,,
9	,,	,,	,,	,,
10	,,	,,	,,	,,
11	,,	,,	,,	,,
12	,,	,,	,,	,,
13	,,	,,	Inverted	,,
14	,,	,,	,,	,,
15	,,	,,	,,	,,
16	,,	,,	,,	,,
17	,,	,,	,,	,,
18	,,	,,	,,	Comparable
19	,,	,,	,,	,,
20	,,	,,	,,	,,
21	,,	,,	,,	,,
22	,,	,,	,,	,,
23	,,	,,	,,	,,
24	,,	,,	,,	,,
25	,,	,,	Flat	T II
26	,,	,,	,,	,,
27	,,	,,	Inverted	T in CR_7
28	,,	,,	,,	,,
29	,,	,,	,,	,,
30	,,	,,	,,	,,
31	,,	Flat	Low	T II
32	,,	,,	,,	,,

CR_7 IN POSTERIOR CARDIAC INFARCTION

The CR_7 lead was recorded in 32 cases during different stages of recovery from posterior infarction, and changes in the T wave were compared with those found in leads II and III (Table I). The diagnosis of infarction was made from the clinical history and examination, and its localization determined from changes in successive cardiograms; in 2 cases a necropsy confirmed it. The T wave was always inverted in lead III. The findings in lead II were impressive, the T wave being inverted in 30 and flat in the remaining 2 cases. The series included patients examined many years after the initial infarction, but in none was T II upright. These findings show that recovery of the T II takes place much more slowly in posterior infarction than in anterior. Among the 32 cases, the T in CR_7 was only normal in 1, and that was taken two years after infarction. It was low in 13, flat in 2, and inverted in 16. In 21 patients the changes in the T wave were greater in lead II than in CR_7 (Fig. 2), in 7 they were comparable, while in 4 the changes in CR_7 were greater than in II (Fig. 3 and 4).

FIG. 4.

FIG. 5.

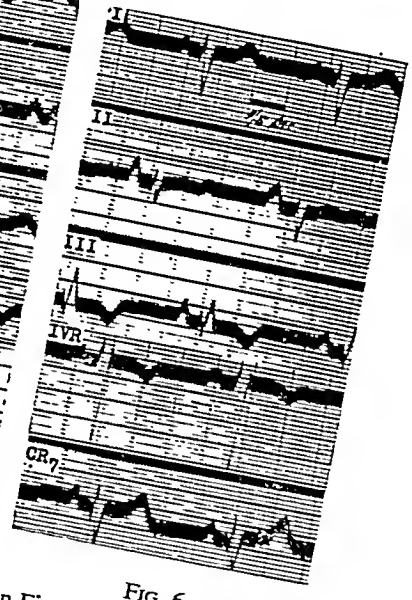

FIG. 6.

FIG. 4.—Posterior cardiac infarction, two months after cardiogram shown in Fig. 3. Slight inversion of T in II and CR_7 now comparable.

FIG. 5.—Anterior cardiac infarction. Male, aged 39. Inversion of T in CR_7 less than in I and IVR, but greater than in II.

FIG. 6.—Heart failure from emphysema. Female, aged 49. T inverted in III and slightly inverted in II, but upright in CR_7. T also inverted in CR_1 and IVR. (See also Fig. 8.)

CR_7 IN ANTERIOR CARDIAC INFARCTION

The CR_7 cardiogram was recorded in 12 patients with anterior infarction at various intervals after the attack, and the T wave compared with that in leads I, II, and IVR (Table II). The T wave was inverted in leads I and IVR in all cases; in lead II it was inverted in 7 and upright in 5, while in CR_7 it was inverted in 9 and upright in 3. In 3 cases where T was upright in lead II, it was inverted in CR_7, but was only once inverted in lead II when it was upright in CR_7. The degree of inversion of the T wave in CR_7 was next compared with that in IVR and I. It was never greater in CR_7 than in IVR and only once was it as great. The inversion of T in lead I was comparable with that in CR_7 in 5, greater than in CR_7 in 6, and less in only 1 case. Thus in anterior cardiac infarction inversion of the T was a commoner finding in CR_7 than in II, but less common and less prominent than in leads IVR and I (Fig. 5).

TABLE II

T WAVE IN CR_7 COMPARED WITH T IN LEADS I, II, AND IVR, IN ANTERIOR CARDIAC INFARCTION

Case No.	State of T wave in limb and chest leads			
	I	II	IVR	CR_7
1	Inverted	Inverted	Inverted	Inverted
2	,,	,,	,,	,,
3	,,	,,	,,	,,
4	,,	,,	,,	,,
5	,,	,,	,,	,,
6	,,	,,	,,	,,
7	,,	,,	,,	,,
8	,,	Upright	,,	Upright
9	,,	,,	,,	,,
10	,,	,,	,,	,,
11	,,	,,	,,	Inverted
12	,,	,,	,,	,,

CR_7 IN OTHER CONDITIONS

Congenital Heart Disease.—In three cases of pulmonary stenosis and in one with atrial septal defect the T wave was inverted in leads II and III, giving to the cardiogram the appearance of the curve characteristic of posterior cardiac infarction. In each instance the T in CR_7 was upright (Fig. 7 and Table III). Admittedly the clinical diagnosis of congenital heart disease was not here in doubt, but in older subjects with cardiographic irregularities from congenital heart disease, and especially in those with pain in the chest, the upright T in CR_7 serves to exclude the presence of cardiac infarction.

TABLE III

T WAVE IN CR_7 AND STANDARD LEADS, IN CONGENITAL HEART DISEASE, EMPHYSEMA, AND PERICARDIAL DISEASE

Case No.	Clinical condition	State of T wave in limb and chest leads			
		I	II	III	CR_7
1	Pulmonary stenosis	Upright	Inverted	Inverted	Upright
2	,, ,, ...	,,	,,	,,	,,
3	,, ,, ...	,,	,,	,,	,,
4	Atrial septal defect	,,	,,	,,	,,
5	Emphysema with heart failure ..	,,	,,	,,	,,
6	,, ,, ,, ..	,,	,,	,,	,,
7	Pericardial disease	,,	,,	,,	,,
8	,, ,, ...	,,	,,	,,	,,
9	,, ,, ...	,,	,,	,,	,,
10	,, ,, ...	,,	,,	,,	,,
11	,, ,, ...	Flat	,,	,,	Flat
12	,, ,, ...	,,	,,	,,	Inverted
13	,, ,, ...	Inverted	,,	,,	,,

Emphysema with Heart Failure.—In many patients with emphysema the cardiogram shows no distinctive changes, but when great enlargement of the heart is conjoined with failure, the limb lead tracing may resemble that found in posterior infarction (Fig. 6 and 8). We examined two such patients whose limb lead cardiograms showed inversion of T II and T III; in both the T in CR_7 was upright supplying evidence that the changes were the result of right heart failure and not posterior infarction. Incidentally, the same help in diagnosis was also given in our two patients by CR_1, which showed inversion of the T wave.

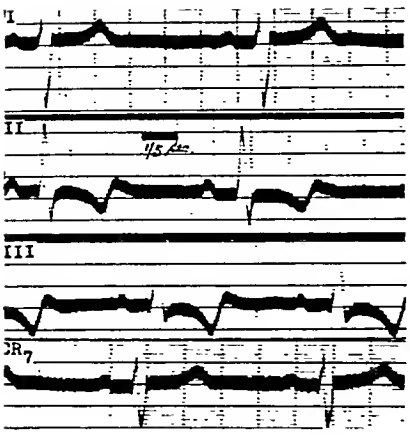

FIG. 7.

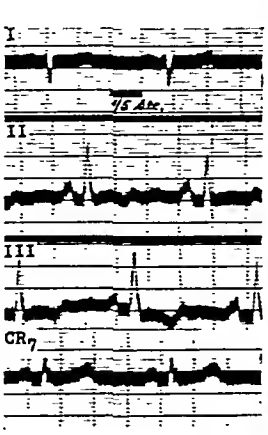

FIG. 8.

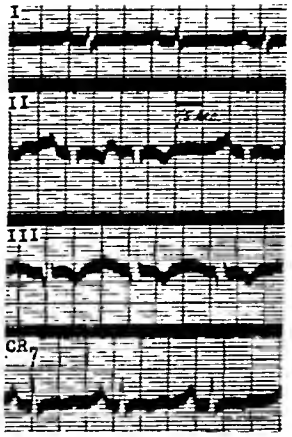

FIG. 9.

FIG. 7.—Congenital pulmonary stenosis. Female, aged 28. T inverted in II and III, but upright in CR_7. T also inverted in CR_1 and IVR.

FIG. 8.—Heart failure from emphysema. Male, aged 39. T inverted in II and III, but upright in CR_7. T also inverted in CR_1.

FIG. 9.—Pericardial disease. Male, aged 32. T inverted in II and III, low in I, and diphasic in CR_7.

Pericardial Disease.—The CR_7 cardiogram was recorded in 7 patients with pericardial disease in whom T II and T III were inverted (Table III); in 3 of these T I was upright when the T in CR_7 was also upright; in 3 the T I was low or flat, when the T in CR_7 was flat in two (Fig. 9) and inverted in the other; in one patient T I was inverted and so was the T in CR_7.

These changes appear to establish that when T II and T III inversion stands for pericardial disease, the T in CR_7 is upright when T I is upright, and inverted when T I is inverted.

Hypertension.—Among 12 cases of hypertension, T I was flat in 2 and inverted in 10. The T in CR_7 was inverted in every case. Changes in the T in other leads were varied, so that in lead II it was upright in 5, low in 2, and inverted in 5; in lead III it was upright in 9 and inverted in 3; in IVR it was upright in 7 and inverted in 5. When the degree of T wave inversion was specially considered in the different leads, in 6 cases it was greatest in CR_7 and I, in 4 cases in CR_7, and in 2 in IVR when the T in CR_7 showed the next most prominent inversion (Table IV).

It is known that the chest lead IVR cannot decide whether changes in the limb lead cardiogram stand for anterior cardiac infarction in a patient with prolonged hypertension. In these cases the T in IVR is sometimes inverted and sometimes upright, and on clinical grounds this change does not appear to depend on the presence or absence of cardiac infarction in addition to hypertension. The chest lead CR_7 does, however, help in the differential diagnosis of anterior infarction and such infarction conjoined with hypertension. Thus in a patient with hypertension when T is inverted in lead I and upright in IVR, the abnormal cardiogram is usually the direct result of the hypertension (Fig. 10). When the T in IVR is inverted, the degree of inversion in CR_7 should be examined; if the inversion is greater in IVR than in CR_7 (Fig. 11), the change is usually due to supervening cardiac infarction, but if the inversion is greater in CR_7 than in IVR, the change is likely to be the result of hypertension alone (Fig. 12).

Aortic Stenosis and Aortic Incompetence.—The changes in aortic stenosis (5 cases) and in aortic incompetence (3 cases) were comparable with those in prolonged hypertension. T in CR_7 was always inverted (Fig. 13), but in other leads it was variable; in lead I it was inverted in 6 and upright in 2; in lead II it was inverted in 5 and upright in 3; in lead III it was upright in 2, flat in 3, and inverted in 3; in IVR it was upright in 2 and inverted in 5, and it was not recorded in another case. When the degree of T wave inversion was compared in the different

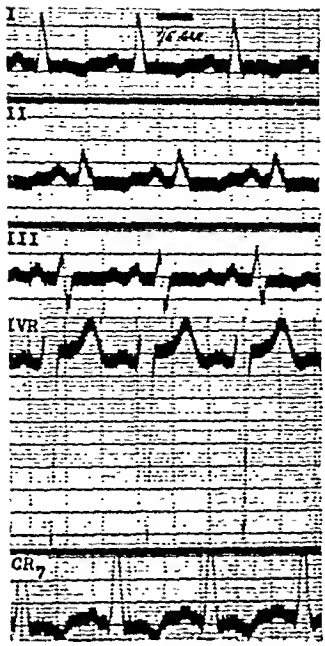

FIG. 10.

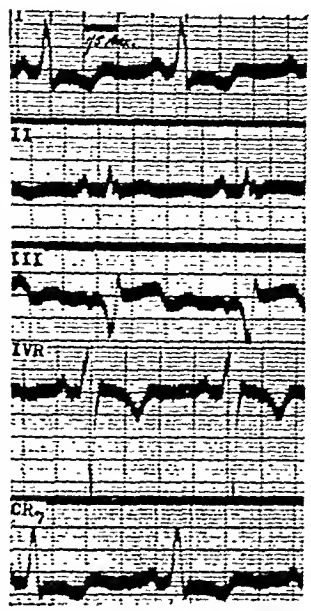

FIG. 11.

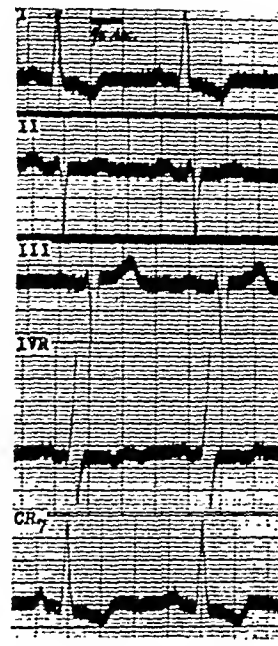

FIG. 12.

FIG. 10.—Hypertension. Male, aged 40. T upright in IVR. Inversion of T greater in CR_7 than in I and II.

FIG. 11.—Hypertension and cardiac infarction. Male, aged 62. T inverted in I and slightly inverted in II. Inversion of T in IVR greater than in CR_7.

FIG. 12.—Hypertension. Male, aged 70. Inversion of T in CR_7 greater than in IVR, and comparable with that in I.

leads it was found that 5 out of the 8 cases showed the greatest change in CR_7 and this finding is almost the same as in hypertension (Table IV).

TABLE IV

T WAVE IN CR_7 COMPARED WITH T IN STANDARD LEADS IN HYPERTENSION AND AORTIC DISEASE

Case No.	Clinical condition	State of T wave in limb and chest leads					Leads showing greatest inversion
		I	II	III	IVR	CR_7	
1	Hypertension	Flat	Inverted	Inverted	Inverted	Inverted	IVR
2	,, ...	,,	,,	,,	Upright	,,	CR_7
3	,, ...	Inverted	Upright	Upright	,,	,,	,,
4	,, ...	,,	,,	,,	Inverted	,,	,,
5	,, ...	,,	Inverted	,,	Upright	,,	CR_7 & I
6	,, ...	,	,,	Inverted	,,	,,	,,
7	,, ...	,,	Low	Upright	,,	,,	,,
8	,, ...	,,	,,	,,	Inverted	,,	IVR
9	,, ...	,,	Inverted	,,	Upright	,,	CR_7 & I
10	,, ...	,,	Upright	,,	Inverted	,,	,,
11	,, ...	,,	,,	,,	,,	,,	CR_7
12	,, ...	,,	,,	,,	Upright	,,	CR_7 & I
13	Aortic stenosis ..	,,	Inverted	Flat	Inverted	,,	II
14	,, ,, ...	,,	,,	Inverted	,,	,,	CR_7
15	,, ,, ...	,,	,,	Upright	Inverted	,,	,,
16	,, ,, ...	Upright	,,	Inverted	,,	,,	IVR & I
17	,, ,, ...	,,	Upright	Flat	Upright	,,	CR_7
18	Aortic incompetence ..	Inverted	,,	Upright	,,	,,	CR_7 & IVR
19	,, ,, ..	,,	,,	Flat	Inverted	,,	III
20	,, ,, ..	,,	Inverted	Inverted	,,	,,	CR_7

Bundle Branch Block.—In 5 cases of left bundle branch block the T wave was inverted in CR_7 (Fig. 14), and it was upright in 4 cases of right bundle branch block (Fig. 15). The T wave in the other leads (limb and IVR) was sometimes inverted and sometimes upright.

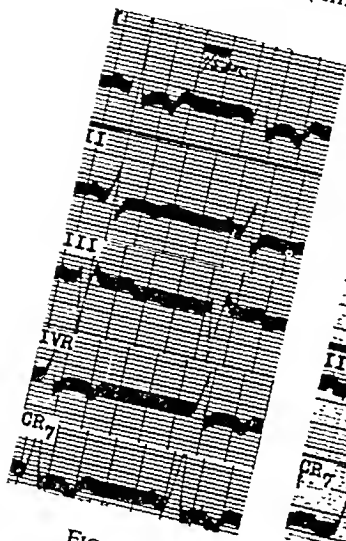

FIG. 13.

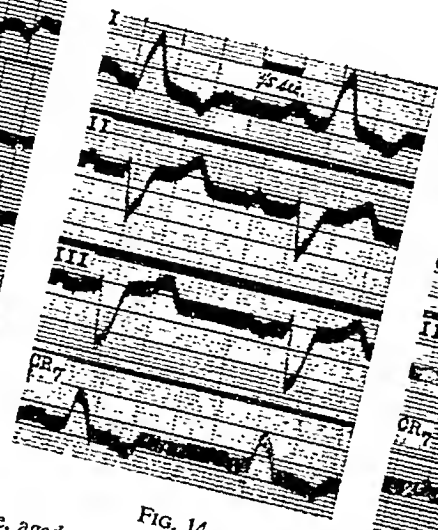

FIG. 14.

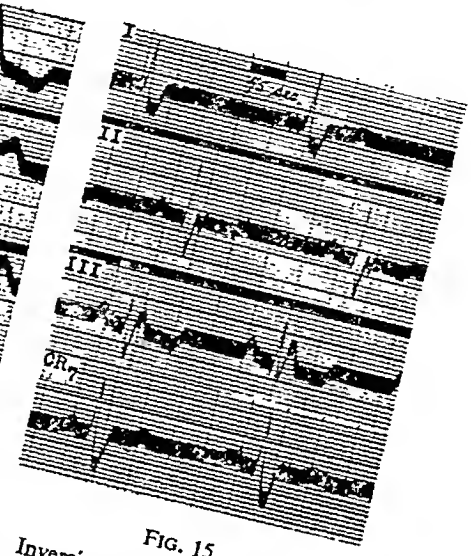

FIG. 15.

FIG. 13.—Aortic stenosis. Male, aged 65. T slightly inverted in II. Inversion of T in CR_7 greater than in IVR, and comparable with that in I.

FIG. 14.—Left bundle branch block. Male, aged 65. T inverted in CR_7.

FIG. 15.—Right bundle branch block. Male, aged 64. T upright in CR_7.

CONCLUSIONS

A new chest lead, CR_7, is described and has been tested in the differential diagnosis of cardiac infarction.

The lead proved to have a limited value in identifying posterior infarction, but it was seldom superior to the limb leads. Indeed our experience has emphasized the importance of T II in posterior infarction, for in 30 out of 32 patients it supplied the evidence necessary for the diagnosis. In contrast, T II in anterior infarction was less reliable, and T in CR_7 was often its superior, although inferior to T in IVR.

CR_7 had greatest value in distinguishing between the T II and T III inversion of posterior infarction and similar changes found in heart failure from emphysema, in pericardial disease, in congenital heart disease, and occasionally in healthy subjects. This new chest lead also helped in the diagnosis of hypertension and aortic valvular disease when complicated by anterior cardiac infarction.

We wish to thank Dr. John Parkinson, Physician to the Cardiac Department, for his helpful criticism of this paper.

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POTASSIUM EFFECTS ON T WAVE INVERSION IN MYOCARDIAL INFARCTION AND PREPONDERANCE OF A VENTRICLE

BY

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The action of potassium on the normal T wave of the electrocardiogram has been established in several species. Wiggers (1930) showed that there was a rise in the normal upright T wave after injection of potassium salts into dogs. Similar results have been found in man after large doses of potassium salts by mouth and intravenously (Thompson, 1939, a & b ; and Keith, Osterberg, & Burchell, 1942). The possibility that changes produced by raising the serum potassium might throw some light on low voltage electrocardiograms led to the investigation of cases of thyroid deficiency (Sharpey-Schafer, 1943). In cases showing T wave inversion in all standard leads, it was found that potassium caused the T waves to become upright. It became necessary, therefore, to investigate the effect of potassium on other forms of T inversion. This paper reports the results obtained in cases with myocardial infarction and cases with preponderance of the left or right ventricle.

Methods.—15 to 20 g. of an equal mixture of potassium chloride and potassium citrate dissolved in about 250 c.c. of water were given by mouth or by stomach tube. Cardiograms were taken before, one to one and a half, and two to two and a half hours after. Chest leads used were IV R, LP–R, RP–R (Wood and Selzer, 1939). Blood samples were taken at the same time as the cardiograms, and serum potassium was estimated by a modification of the method of Kramer and Tisdall (1921). A few subjects showed little or no change in the serum potassium and cardiogram after these doses of salt, and there was considerable individual variation in response, as has been noted by Keith, Osterberg, and Burchell (1942). Successful observations were made in the following: 4 cases with T III pattern myocardial infarction, 4 with T I pattern myocardial infarction, 9 with T inversion due to left ventricular preponderance, and 4 with T inversion due to right ventricular preponderance.

Results

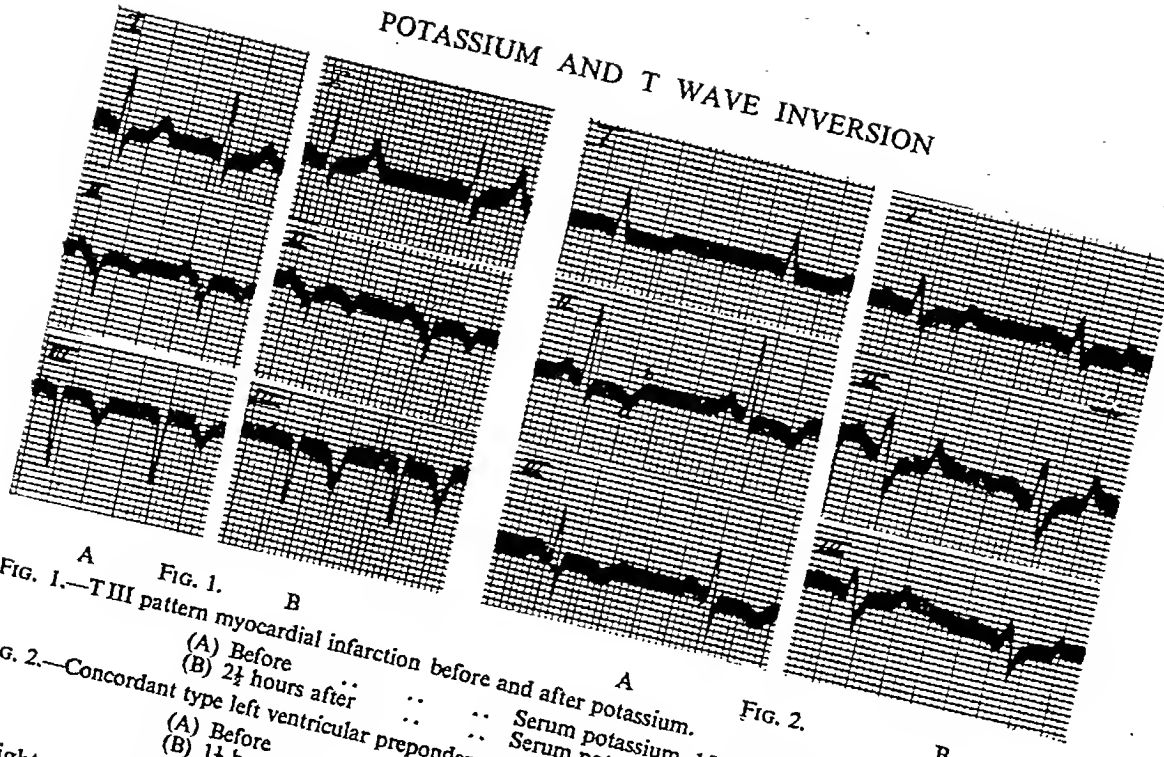
Throughout each group the results were the same.

T III pattern myocardial infarction.—T III became more inverted and T I more upright (Fig. 1). The three chest leads, as expected, became more upright.

T I pattern myocardial infarction.—T I became more inverted and T III more upright (Fig. 3). T IV followed T I, and S–T elevation was often accentuated. The original pattern of each case was not, however, changed.

Left ventricular preponderance with T I and T IV inverted.—In comparison with T I pattern cardiograms the effect of potassium was exactly opposite, T I and T IV becoming upright (Fig. 4).

Left ventricular preponderance, concordant type.—In this type of case, usually aortic stenosis or hypertensive heart disease, T waves are apparently inverted in all standard leads, and QRS may show no axis shift. The effect of potassium is to throw all T waves sharply



A B

FIG. 1.—T III pattern myocardial infarction before and after potassium.
(A) Before .. .. .. Serum potassium, 15 mg. per 100 c.c.
(B) 2½ hours after .. .. .. Serum potassium, 23 mg. per 100 c.c.

A B

FIG. 2.—Concordant type left ventricular preponderance. Aortic stenosis.
(A) Before .. .. .. Serum potassium, 23 mg. per 100 c.c.
(B) 1½ hours after .. .. .. Serum potassium, 36 mg. per 100 c.c.

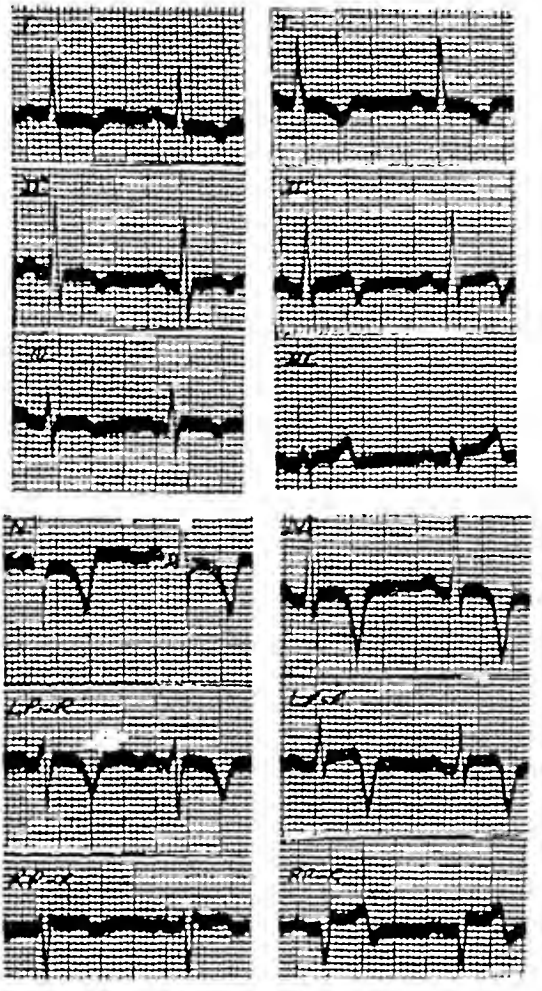
upright, while the upward-curved S–T depression remains or may even be accentuated (Fig. 2).

Right ventricular preponderance.—Three cases of chronic cor pulmonale, due to emphysema, were investigated. Results were similar to those found in left preponderance. T inversion, best seen in the chest leads, became upright after potassium (Fig. 5). A similar striking result was seen in a case of acute cor pulmonale due to a packed pulmonary embolism (to be published elsewhere).

Other effects of potassium.—Flattening of the P waves and widening of QRS occurred when the rise of serum potassium was great. Similar changes with the same degree of serum potassium rise have been reported in dogs by Hoff, Smith, and Winkler (1941). No patient with myocardial infarction complained of chest pain after potassium, and no patient showed rhythm changes.

DISCUSSION

The results of this investigation indicate that raising the serum potassium may prove a valuable method in the practical analysis of the electrocardiogram. Curves are often seen that are difficult to interpret without serial observation over long periods, while giving potassium salts by mouth offers the possibility of interpretation within a few hours. The safety of the procedure needs some discussion. Hoff, Smith, and Winkler (1941) have shown that death may result in dogs when the serum potassium is trebled, and from levels observed in cases of uræmia similar results might be expected in man. In our series the greatest rise of serum potassium was from 21 mg. to 38 mg. per 100 c.c. of serum. Several of the subjects with hypertensive heart disease had impairment of renal function, while several others had congestive heart failure. It might be wise, however, to exercise caution in patients suspected of having myocardial infarction, since Katz and Linder (1938) have shown that potassium diminishes coronary flow. 10 g. or less of potassium salts might be given to such patients as a preliminary trial to determine individual response. Both Thompson (1939b) and Keith, Osterberg, and Burchell (1942) thought that cardiographic changes did not follow strictly



A FIG. 3. B

FIG. 3.—T I pattern myocardial infarction before and after potassium.

(A) Before .. .. .. Serum potassium, 20 mg. per 100 c.c.
(B) 1 hour after .. .. Serum potassium, 27 mg. per 100 c.c.

the rise in serum potassium. Consideration of their published figures and our own data suggest that the evidence is not sufficient to warrant an opinion. In general, the opinion of Hoff, Smith, and Winkler, that the cardiogram follows the serum potassium, seems correct. The theoretical aspect presents great difficulties. Fenn (1940), reviewing the physiological role of potassium, has stressed our ignorance of electrolyte exchange. Joseph, Cohn, and Greenberg (1939), using radioactive potassium, showed that most of the ingested potassium was taken up by the liver, and that the rise in extracellular fluids preceded by some hours the rise in cells. It is possible that cardiographic changes produced by these doses of potassium salts result solely from electrolyte changes in the extracellular fluids or in the general " conducting medium " to the periphery of which leads are attached. Yet potassium presumably affects the heart itself, as numerous workers since Blake (1839) have shown that standstill and death result from excess. Careful inspection of our results reveals no evidence that potassium produces specific changes in the normal or abnormal cardiogram, as, for example, does digitalis. The effect, so far as S–T interval and T wave are concerned, appears to be an accentuation of deflections that are already present. Thus S–T deviation rather than deepen-

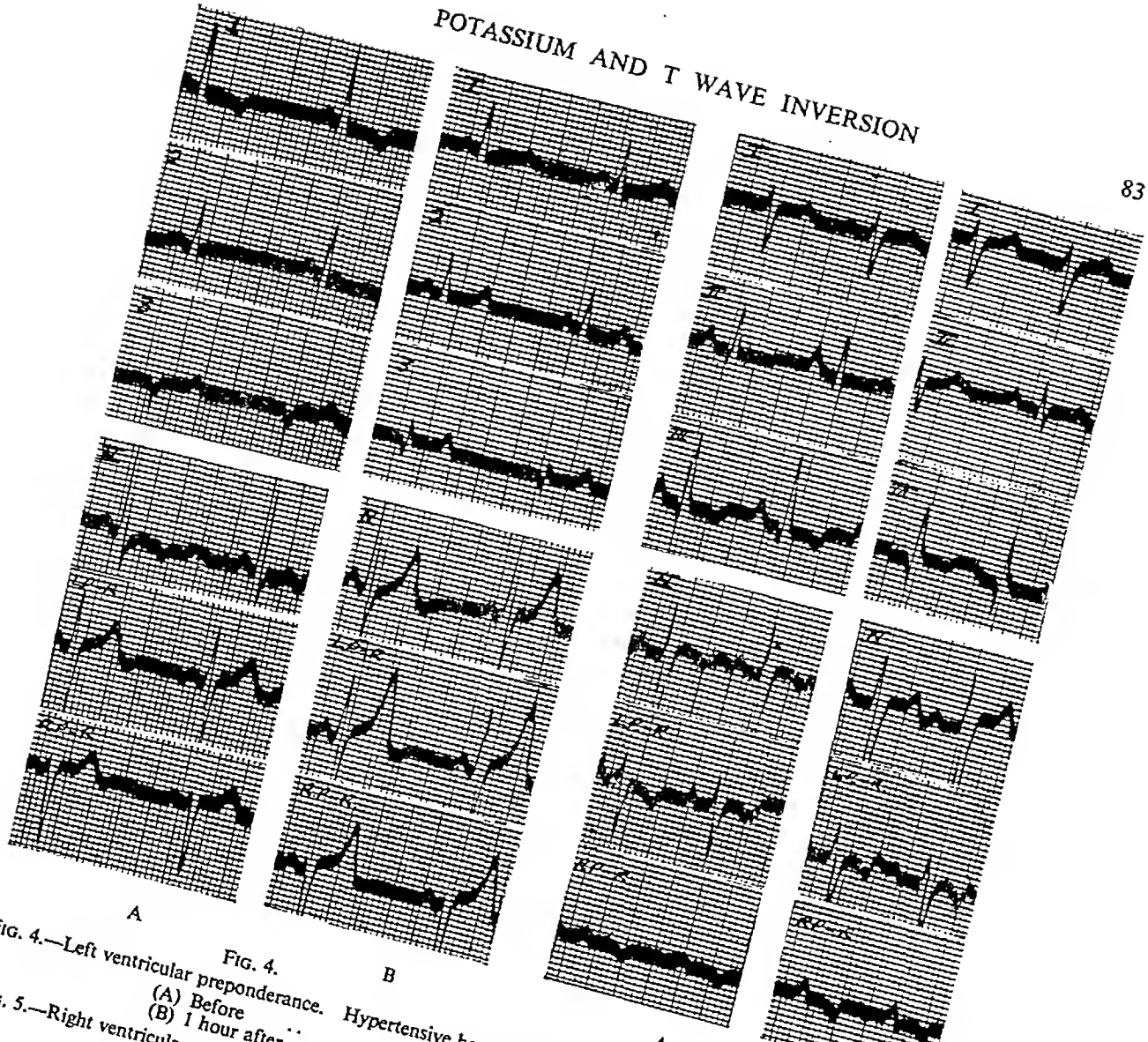


FIG. 4. FIG. 5.

FIG. 4.—Left ventricular preponderance. Hypertensive heart disease.
(A) Before .. .. Serum potassium, 19 mg. per 100 c.c.
(B) 1 hour after .. .. Serum potassium, 26 mg. per 100 c.c.

FIG. 5.—Right ventricular preponderance. Chronic cor pulmonale from emphysema.
(A) Before .. .. Serum potassium, 20 mg. per 100 c.c.
(B) 24 hours after .. .. Serum potassium, 23 mg. per 100 c.c.

ing of the T wave would be expected in cases of myocardial infarction, were potassium to cause further acute ischæmia of the myocardium. The theory of the normal and abnormal deflection of retreat in the human cardiogram is still obscure. Interpretation is therefore necessarily empirical. The effect of potassium on simple systems consisting of muscle strips in a conducting medium, such as those described by Craib (1930) has not apparently been studied. However, the results obtained on "T inversion" in preponderance of a ventricle are of some theoretical interest. Most workers would agree that this inversion is a fundamentally different mechanism from that seen in disease of the coronary artery. The appearance of an upright T wave after potassium suggests that inversion in preponderance of a ventricle may be an S–T rather than a T wave change and that in Fig. 2, lead II, the point "b" rather than "a" is the apex of the T wave. In some curves this is substantiated by Q–T measurements, but, in view of QRS widening and other factors after potassium, considerably more evidence is required before such measurements can be analysed.

SUMMARY

T wave inversion due to myocardial infarction is further inverted by raising the serum potassium, while T wave inversion due to preponderance of a ventricle becomes upright after potassium.

The method is useful in analysis of difficult electrocardiograms. It is suggested that T inversion in ventricular preponderance is an S–T change, not a T wave change.

Serum potassium was estimated in the School laboratories (Director, Dr. E. J. King). My thanks are due to the Chief Medical Officer, L.C.C., for permission to publish the clinical material.

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POTASSIUM EFFECTS ON THE ELECTROCARDIOGRAM OF THYROID DEFICIENCY

BY

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As there is no method for detecting and measuring circulating thyroid hormone, indirect investigations have to be used for the accurate diagnosis of thyroid deficiency. It is difficult to obtain evidence that thyroid deficiency in man is complete. In addition to the ordinary metabolic and biochemical findings, the response to injected pituitary thyrotrophic hormone must be negative (Sharpey-Schafer and Schrire, 1939), histological changes are present in the pituitary gland, and there is possibly an excess of thyrotrophic principle in the circulating blood (Collard, Mills, Rundle, and Sharpey-Schafer, 1940). Clinical observations may be quite indecisive. The cardiogram, however, affords a valuable measure. Elsewhere, evidence will be given that when thyroid deficiency is complete, reversible cardiographic changes are always present. The changes show a constant picture: in addition to a general low voltage, the T waves are flat or in a few cases inverted. It can usually be proved that thyroid deficiency is not complete in cases that do not show a typical cardiogram, though the presence of a classical one does not necessarily imply that the patient is strictly comparable to a thyroidectomised animal. The action of thyroid hormone on such cardiograms is well known. Provided a sufficient dosage is given, the appearances return to those which are normal for the individual. Of special interest are those rarer cases with T wave inversion. Thyroid causes such T waves to become upright, yet their presence is sometimes mistaken for conditions such as coronary arterial disease. Any other method of altering the cardiogram of thyroid deficiency might throw some light on its mechanism and prove of value in the differential diagnosis of low voltage curves generally. This paper reports the effect on such cardiograms of raising the serum potassium.

MATERIAL

The procedure is reported elsewhere (Sharpey-Schafer, 1943). Many patients showed a later rise of serum potassium than others without thyroid deficiency, possibly due to a slower rate of absorption from the intestine. The evidence for thyroid deficiency in 12 patients is given in the Table. Signs and symptoms are those given in the *Report on Myxœdema*, 1888, a description that has not been bettered. The measurement of response to thyrotrophic hormone has been previously published (Sharpey-Schafer and Schrire, 1939). Many cases received very large doses of pituitary extract. A biopsy of the thyroid is available in Case 1, and post-mortem material in the untreated state in Case 7. There was clear clinical and other evidence in Case 4 that thyroid deficiency was not complete; the cardiographic changes were, however, similar to those found in cases of proved complete deficiency. The patient with Addisonian anæmia (see Fig. 3) on the occasion of the observation had 1,100,000 red cells per c.mm. and 24 per cent hæmoglobin. The venous pressure was raised, and pitting œdema was present.

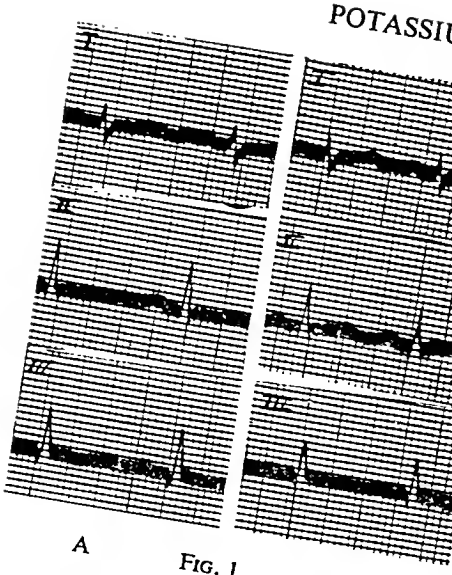
TABLE

SUMMARY OF GENERAL FEATURES AND OF SIZE OF T WAVES BEFORE AND AFTER TREATMENT

Case	Age Sex	Symptoms and signs	B.M.R. per cent	Cholesterol mg. per 100 c.c.	Response to thyrotrophic hormone	Size of T waves in electrocardiogram (millivolts)					
						Untreated		After potassium		After treatment with thyroid	
						Upright	Flat or Inverted	Upright	Flat or Inverted	Upright	Flat or Inverted
1	F. 20	+	−26	150–315	0	I 0·05					
2	F. 70	+	−34	254–353	0		II 0·00 III 0·00	I 0·10 II 0·10	III 0·00	I 0·13 II 0·23 III 0·05	
3	F. 40	+	−26	150–290	0		I 0·00 II 0·05 III 0·10	I 0·05 II 0·04	III 0·00	I 0·12 II 0·20 III 0·10	
4	F. 49	±	−31 to −37	335–400	sl.+		I 0·10 II 0·12 III 0·05	I 0·10 II 0·13	III 0·00	I 0·20 II 0·20	III 0·00
5	F. 10	+	−27	415	0	I 0·03 II 0·07 III 0·02	I 0·05 II 0·10 III 0·15	I 0·10 II 0·05	III 0·05	I 0·15 II 0·40 III 0·25	
6	F. 48	+	−36 to −46	180	0			I 0·08 II 0·20 III 0·10		I 0·15 II 0·22 III 0·10	
7	F. 63	+	−41	270–290	0		I 0·00 II 0·00 III 0·00	I 0·02 II 0·10 III 0·05		I 0·13 II 0·20 III 0·10	
8	F. 58	+	−32	217	0	II 0·10 III 0·10	I 0·00	I 0·10 II 0·20 III 0·13		I 0·10 II 0·20 III 0·13	
9	F. 59	+	−15	184	0	I 0·02	II 0·00 III 0·05	I 0·20 II 0·15	III 0·05	I 0·30 II 0·30	III 0·00
10	F. 66	+	−34	296	0	III 0·05	I 0·05 II 0·00	II 0·10 III 0·13	I 0·00	I 0·15 II 0·15	III 0·00
11	F. 66	+	−32	270	0		I 0·00 II 0·00 III 0·00	I 0·10 II 0·20 III 0·05			
12	F. 41	+	−32	270–310	0		I 0·00 II 0·00 III 0·00	I 0·04 II 0·10 III 0·05			
							I 0·00 II 0·00 III 0·00	I 0·02 II 0·07 III 0·05	I 0·10 II 0·15 III 0·05		

RESULTS

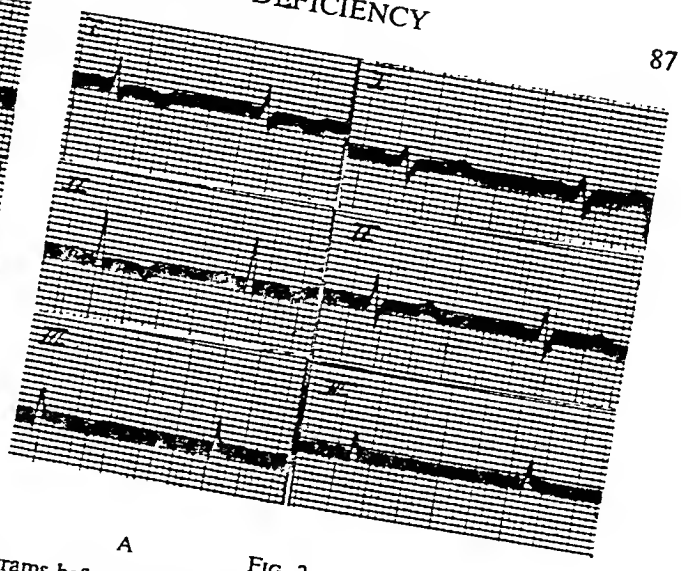
The results are shown in the Table. T wave voltage after treatment with thyroid is given in the last column. All cases showed the same change to a greater or lesser degree. Those with flat T waves showed a rise of the T wave after potassium (Fig. 1). If the T waves were inverted, they also became upright (Fig. 2). The case with Addison's anæmia (Fig. 3) showed a different change. The control cardiogram cannot be distinguished from one due to thyroid



A B

FIG. 1.

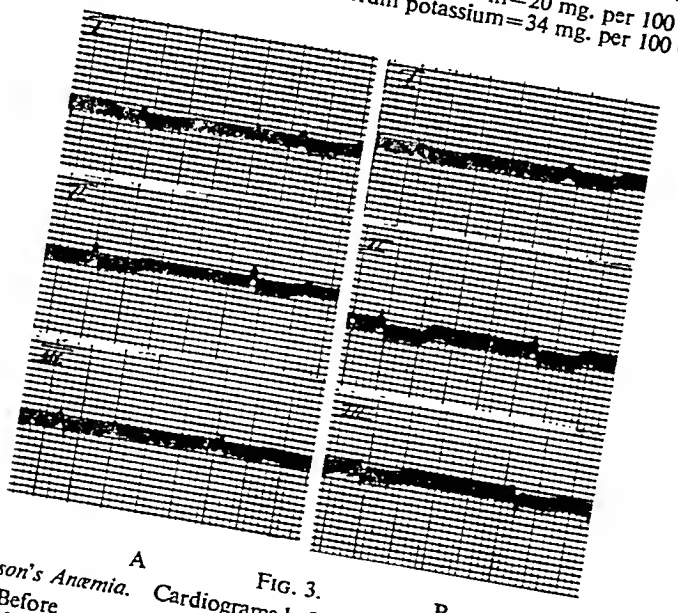
FIG. 1.—*Case* 1. *Myxœdema.* Cardiograms before and after treatment with potassium.
(A) Before .. .. .. Serum potassium=20 mg. per 100 c.c.
(B) 1½ hours after .. .. Serum potassium=25 mg. per 100 c.c.



A B

FIG. 2.

FIG. 2.—*Case* 3. *Myxœdema.* Cardiograms before and after treatment with potassium.
(A) Before .. .. .. Serum potassium=20 mg. per 100 c.c.
(B) 2¼ hours after .. .. Serum potassium=34 mg. per 100 c.c.



A B

FIG. 3.

FIG. 3.—*Addison's Anæmia.* Cardiograms before and after treatment with potassium.
(A) Before .. .. .. Serum potassium=22 mg. per 100 c.c.
(B) 2¼ hours after .. .. Serum potassium=28 mg. per 100 c.c.

deficiency, especially since the heart rate is relatively slow. After potassium S–T depression is accentuated without much change in the T wave.

DISCUSSION

The results indicate that the effect of potassium on the T wave of thyroid deficiency is similar to the effect of thyroid hormone. The time taken for action is, however, very different for the two substances. While potassium produces changes in a few hours, thyroid takes

days. It is not suggested that there is any direct connection between these two effects. The serum potassium in cases of thyroid deficiency lies within normal limits, and, although the voltage of the normal T wave may be lowered by lowering serum potassium (unpublished data), there is no evidence that cardiographic appearances in hypothyroidism are due to electrolyte changes. It is possible that potassium merely accentuates deflections that are already present, so far as S–T interval and the T wave are concerned (Sharpey-Schafer, 1943). If this is so, the results described here suggest that no fundamental change in pattern is involved in the production of the cardiogram of thyroid deficiency. Since the first report by Zondek (1918) numerous authors have written on the cardiographic findings in myxœdema. Ohler and Abramson (1934), reviewing such papers and reporting on 35 cases, discussed the following possible causes: (1) sclerosis of the coronary arteries, (2) anæmia, (3) cardiac dilatation and sluggishness, (4) vagal stimulation, (5) cutaneous resistance, and (6) pericardial effusion. They showed that there was good evidence against causes (2), (3), (4), & (5), and, since potassium further inverts the T wave of myocardial infarction, our findings support Ohler and Abramson in dismissing cause (1). Indeed, T inversion in hypothyroidism responds to potassium in the same manner as T inversion in preponderance of a ventricle. We have post-mortem evidence in untreated cases that the classical cardiogram can occur in the absence of pericardial effusion. The effect of potassium on the cardiogram of pericarditis has not yet been investigated.

Summary

The flat T wave of thyroid deficiency became upright after potassium. Inverted T waves also became upright, a response which is similar to that in preponderance of a ventricle and unlike that of myocardial infarction. A case of Addison's anæmia showed accentuation of the S–T depression.

Biochemical estimations were made in the School laboratories (Director, Dr. E. J. King). My thanks are due to Dr. Alison Macbeth, of Organon Ltd., for generous supplies of thyrotrophic extract, and to the Chief Medical Officer, L.C.C., for permission to publish the clinical material.

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ANGINAL PAIN IN MYXŒDEMA

BY

A. A. FITZGERALD PEEL

Received November 17, 1942

It has long been recognized that myxœdematous patients beyond middle life may suffer from arteriosclerosis, hypertension, or coronary disease in addition. Until recent years it seems to have been accepted that anginal pain in a myxœdematous patient was evidence of some such complication. Inasmuch as non-myxœdematous angina pectoris is sometimes greatly relieved by the development of spontaneous or post-operative myxœdema, it has been generally concluded that treatment of a myxœdema with thyroid is likely to aggravate any co-existing anginal pain. Since 1924, however, isolated reports have appeared describing myxœdematous patients whose anginal pain improved on treatment with thyroid. Fournier (1942) found six cases recorded, and he appears to have overlooked three—one by Campbell and Suzman (1934) and two by Zondek (1941). The time would therefore seem to be ripe for a review of the whole subject of anginal pain in myxœdema.

Zondek (1918), in his original description of the "myxœdema heart" mentions slight precordialgia as one of the less frequent symptoms. Laubry *et al.* (1924) record a patient, aged 47, who had "for three years suffered from anginal crises daily or several times a day, brought on by the slightest effort"; there was typical myxœdema but no evidence of independent heart disease. Treatment with thyroid caused rapid disappearance of the anginal crises *pari passu* with reduction in the size of the heart. The patient was observed for ten years (Fournier, 1942) during which he suffered from anginal pain only when treatment with thyroid was discontinued.

A slightly different syndrome is illustrated by one of Campbell and Suzman's (1934) cases. They discuss the cardiovascular findings in eight cases of myxœdema, of whom two (Cases 7 and 8) had precordial pain; both had anomalous cardiograms, and both were thought to have independent heart disease. Case 7 had typical angina of effort which seems to have been aggravated when thyroid was given. Case 8 complained of "continuous precordial aching made worse by exertion"; this pain disappeared completely as the heart became reduced in size under the influence of thyroid. The drug was later withdrawn without the patient's knowledge; the pain returned after an interval, and its reappearance coincided with the recurrence of cardiac enlargement.

Beach (1935) describes a woman with myxœdema, who suffered, first from a feeling of oppression in the chest, and later from attacks of severe pain; they were induced by exposure to cold and relieved by amyl nitrite; she had T I inversion in her cardiogram and was thought to have independent heart disease. The attacks occurred with increasing frequency until she was having as many as eight daily, and she refused to allow her arms or chest to be uncovered for examination. Within a week of commencing thyroid therapy the attacks ceased. She was under treatment for several years during which attacks occurred only when her basal metabolic rate fell below −20 per cent.

The cases of Beaumont and Robertson (1939) and of Zondek (1941) illustrate yet another syndrome, which has been designated by Zondek "the abortive myxœdema heart." These patients had no obvious clinical signs of myxœdema, but they had a low basal metabolic rate and a raised blood cholesterol. They complained of continuous precordial or sternal tightness

and distress; in addition, they had more or less frequent attacks of collapse with pallor, cold sweating, and a feeling of oppression in the chest. The cardiovascular findings were consistent with a myxœdema heart—enlargement of varying degree, a tendency to bradycardia and low blood pressure, and a small pulse. The cardiogram was normal in some cases, typical of myxœdema in others; T I was occasionally inverted. Nevertheless independent heart disease was thought to be absent in all. Thyroid in doses between 0·5 and 0·7 gram weekly relieved all the symptoms, while no other form of treatment seemed to be of much avail. Additional cases of anginal pain relieved by thyroid are recorded by Ziskin (1930) and Benestad (1937), but it has not been possible to obtain access to their publications.

Fournier (1942) divides cases of myxœdema with angina into two groups. When independent heart disease is present, he states that thyroid will aggravate pre-existing pain, or may induce pain in patients previously free from it; but several of the cases quoted above show that this statement is not true of all cases. In the absence of independent heart disease, he considers the anginal pain is amenable to thyroid therapy. He goes on to discuss the ætiology of the pain in this group; as five of the six cases reviewed were over 40, early coronary disease was difficult to exclude, and he believes that the angina was a response to a mixed pathogenesis. He suggests that these patients had minor coronary lesions, insufficient to produce angina in themselves but capable of doing so in the presence of superadded "myxœdematous lesions." These might take the form of mucinous infiltration of the nervous or vascular elements of the heart, of vagotonia, of hypoglycæmia, or of anæmia. Thyroid therapy, by abolishing the myxœdematous lesions, restores the "status quo" and relieves the anginal pain. In support of this theory he states that some adults with myxœdema show inversion of T I, or of T I and T II; while this may often be corrected by thyroid therapy, it invariably recurs after an interval despite continued treatment. The initial inversion is attributed to a combination of minimal coronary lesions with myxœdematous lesions, the temporary improvement to removal of the myxœdematous lesions, and the ultimate recurrence to progress of the coronary lesions.

There is much that is attractive in Fournier's ideas, and a close analogy exists in the case of patients with early coronary disease complicated by anæmia, in whom cure of the anæmia (whether by liver or by iron) may abolish anginal pain for a time. It is clear that, if this view is justified, any fundamental pathological difference between his two groups of cases disappears; the distinction becomes a matter of degree. The possibility is immediately opened that patients with somewhat more advanced coronary disease might also on occasion derive benefit from treatment with thyroid, as seems to have occurred in the cases of Campbell and Suzman, and of Beach. The problem as to why one patient should be relieved by thyroid while the next is made worse remains unsolved. One explanation seems to have been overlooked. Thyroid, by increasing the circulation rate throws a greater load on the heart, and this will tend to aggravate anginal pain; on the other hand an increase in the general circulation rate will lead to an increased coronary circulation rate unless the vessels are completely occluded, an effect which will tend to relieve anginal pain. The effect in any given patient will thus depend on which of the foregoing factors predominates; and it may well be that each patient has an "optimum" basal metabolic rate and circulation rate at which his anginal pain is minimal.

It may be noted that at least two distinct varieties of pain are represented among the cases quoted. The first is a typical angina of effort, the second a constant pain or ache made worse by effort; the latter type may or may not be accompanied by attacks of collapse. It is important to determine whether any other clinical variety of pain is encountered in myxœdematous patients, and if so, how these patients react to thyroid. In assessing the effect of thyroid, various possibilities must be taken into account. Thus development of pain during thyroid therapy might be due to the action of the drug on the circulation or to a purely coincidental coronary occlusion; disappearance of pain might be due to spontaneous

improvement after a coronary occlusion. The blood picture requires consideration inasmuch as cure of an anæmia can *ipso facto* cause disappearance of effort angina in cases of early coronary disease. Finally the possibility of psychogenic pain cannot be ignored.

The case histories of some sixty myxœdematous patients have been studied. Some of them have been hospital out-patients, some have been seen in private practice, and some have been hospital in-patients under the care of Dr. Angus Scott. I am much indebted to him for permission to make use of the records.

Angina of Effort in Myxœdema

Twelve myxœdematous patients experienced typical angina of effort at some period. Of the twelve, ten had some form of independent heart disease—hypertensive in five, coronary in four, and an intermittent partial block of uncertain ætiology in one. In two cases the findings were consistent with an uncomplicated myxœdema heart. An additional patient who presented a curious mixture of thyrotoxic and myxœdematous symptoms also had an effort angina.

Five patients had *hypertensive heart disease* complicating myxœdema. One of them had diabetes as well; as she required insulin, thyroid was thought to be contra-indicated. One patient failed to report back and cannot be traced. The remaining three (Cases 1, 2, and 3) first complained of anginal pain while on treatment with thyroid. Case 1 had an uncomplicated myxœdema heart when she was first put on thyroid, but two years later she developed a mild hypertension with a slight anæmia; she still had no effort angina. She developed effort angina five weeks after her dose of thyroid was increased from 2 to 3 grains daily; the pain became much less severe and less frequent immediately the dose was reduced again to 2 grains daily. In Cases 2 and 3, angina of effort developed independently of any change in the dose of thyroid; Case 2 had been on treatment for three years, Case 3 for three months. In both the pain improved (in Case 3 it disappeared) although treatment with thyroid was continued; and in both there was some other feature to suggest a coronary occulsion—a diphasic T IV in the cardiogram of Case 2, and a temporary fall in blood pressure while effort angina was present in Case 3.

Four patients were considered to have *coronary disease* complicating myxœdema; all had inversion or partial inversion of T I in the cardiogram. In one I was afraid to order thyroid; another has not been traced. Case 4 had mild hypertension with slight hypertrophy of the left ventricle and calcification of the aorta, as well as T I inversion. She has been on treatment since February 1939; her effort angina is for all practical purposes abolished when she is on a dosage of 3 grains of thyroid daily, but it returns soon after she attempts to discontinue treatment. There has been no demonstrable change in her heart radiologically or cardiographically, and her hæmoglobin percentage is unaltered at 84 per cent; her blood pressure now is 155/105 as compared with 190/90 in February 1939. Unless the disappearance of the effort angina is attributed to psychological factors, which seems unlikely, it is reasonable to conclude that it is due to an improvement in the coronary circulation accompanying an increase in the general circulation rate. With her present dosage of thyroid (3 grains daily), her basal metabolic rate is still −32 per cent; despite this, she is mentally bright and able for much of her housework. Case 5 had suffered from effort angina before thyroid therapy was commenced, and she had inversion of T I and T II in the cardiogram. After a preliminary spell of rest and iron therapy, treatment with elityran was commenced while she was still confined to bed; the drug had to be discontinued after three days owing to complaint of "severe bursting pains in the arms." During the following fortnight changes developed in the cardiogram suggesting that the attack of pain was due to a coronary occlusion. Subsequent resumption of treatment with thyroid had no apparent effect on her angina of effort despite a rise in blood pressure from 145/95 to 170/100; in this respect she resembles Cases 2 and 3.

One patient had myxœdema with an *intermittent partial block* of uncertain ætiology (Case 6). Apart from the intermittent block, the cardiovascular findings were consistent with a myxœdema heart. Block appeared on two occasions, first a week after thyroid treatment was commenced, the second time when she was having no thyroid two years later. For a period of two years she attended irregularly, for three or four weeks at a time at intervals of four to six months; during each spell of attendance she received 2 grains of thyroid daily and her anginal pain improved. She ceased attending in 1937, subsequently visiting many doctors and receiving various forms of treatment other than thyroid; she continued to suffer from effort angina until 1940 when there seems to have been spontaneous improvement in her myxœdema. She has had no anginal pain since, there are no obvious clinical signs of myxœdema now, and her basal metabolic rate is +5 per cent.

Two patients had uncomplicated *myxœdema heart* with angina of effort. The first, a man of 56 whose chief complaint was angina of effort, only returned once, ten days after starting treatment; he said he was " much improved." Case 7 originally had the features of Zondek's " abortive myxœdema heart "; thyroid treatment was advised, but she escaped it by changing her doctor. She has so far had no thyroid, and in the 3 years that have elapsed the character of her pain has altered; it is now a typical angina of effort. There has been an insignificant rise in blood pressure (from 142/85 to 150/95); and she has a mild hypochromic anæmia (hæmoglobin 78 per cent, erythrocytes 5·4 million). It is questionable whether the inverted U waves which have developed should be regarded as indicating coronary disease, thus explaining the change in the character of her pain; alternatively the anæmia may provide the explanation.

One patient with a *mild myxœdema developed a spontaneous thyrotoxicosis* at the menopause (Case 8) and she now has a curious mixture of thyrotoxic and myxœdematous symptoms. The onset of the thyrotoxicosis was accompanied by development of an effort angina which was still present when she was examined a year later.

Discussion

To sum up, angina of effort appeared in one myxœdematous patient who developed a spontaneous complicating thyrotoxicosis, and in four who had independent heart disease during treatment with thyroid. In one of these, the angina developed shortly after an increase in the dosage of thyroid and it improved immediately the dose was reduced to its former level though pain did not completely disappear. In the remaining three the angina seems to have been brought on by a coronary occlusion which was almost certainly coincidental in two cases, though it may have been due to some unexplained action of the drug in one. In none of these three cases was there any aggravation of the anginal pain on subsequent resumption of thyroid therapy; on the contrary, the pain ultimately disappeared in one patient, in a second it improved, while in the third it was unaltered. Angina of effort was abolished by suitable dosage of thyroid in a patient with myxœdema, hypertension, aortic calcification, and coronary disease; the findings in this case suggested improvement in the coronary circulation secondary to an increase in the general circulation rate as the most likely explanation of the disappearance of the pain. A patient with a myxœdema heart complicated by an intermittent partial block showed improvement during each of several short spells of thyroid therapy, and her anginal pain ultimately disappeared when she made an apparently spontaneous recovery from her myxœdema. The effect of thyroid in the two patients with uncomplicated myxœdema heart cannot be gauged as one avoided treatment while the other was under observation for too short a period.

Consideration of the foregoing facts suggests that, even when coronary disease is present, a suitable dose of thyroid may lead to improvement in the coronary circulation and to disappearance of anginal pain. An increase in dosage may cause a disproportionate increase in the general circulation rate and so aggravate the pain. The presence of hypertensive

disease or coronary disease with angina of effort does not contra-indicate the use of thyroid in a myxœdematous patient; but the drug should be given with caution, beginning with a small dose, and an attempt should be made to find the "optimim dosage" for that particular patient. I would make an exception to this rule only in cases of recent coronary occlusion, where it seems reasonable to withhold thyroid until the stage of convalescence has been reached; resumption of thyroid therapy at that stage has not aggravated the pain in any of the cases in this series.

Since writing the foregoing, my attention has been drawn to an article by Phillips and Milliken (1939). Discussing thyroidectomy for angina pectoris, they say: "It is not advisable to recommend thyroidectomy if the basal metabolic rate is less than −15 per cent. The anginal syndrome may be improved by elevating the metabolic rate in some cases with a low basal metabolic rate and low blood pressure. The mechanism is an improvement in the coronary circulation."

Zondek's Abortive Myxœdema Heart

Two examples of this syndrome have been encountered. As it is somewhat rare, a more detailed description of the cases is given in the Table. Reference has already been made to Case 7 who escaped thyroid treatment; 3 years later her pain has altered in character, and she now has a typical effort angina. In Case 9, the clinical features of myxœdema were wanting when she was first seen, and the atypical behaviour of the pain led to a diagnosis of neurosis. Five years later she returned with obvious clinical signs of myxœdema and with the same pain. Her pain improved with a dosage of 2 or 3 grains of thyroid daily, and at times she was quite free from it on this dose; but she was unable to tolerate doses of 4 grains daily. In this respect she shows an analogy with the cases described in the previous section despite the fact that no independent heart disease can be demonstrated; she is aged 58. Her attacks of collapse have also been abolished since treatment was instituted five months ago, except for one occasion when an attack followed painting of the abdomen with strong iodine in preparation for an operation. It is clear that she is sensitive to iodine as well as to thyroid, as she had a well-marked iodine rash on the following day. It is possible that this attack was allergic or anaphylactic in nature; but its close resemblance to her earlier attacks suggests an alternative explanation, namely that absorption of iodine from the skin disturbed her somewhat delicate thyroid balance.

Attacks of Spasmodic Angina in Myxœdema

Two myxœdematous patients described attacks which suggested simple spasmodic angina. Case 10 had osteoarthritis of the spine, and had suffered from a more or less constant pain in the left side of her back radiating through to the front for many years before she developed any myxœdematous symptoms. This pain was unaffected by thyroid treatment. She had developed symptoms of myxœdema some nine months before she first attended, and during that period she had five attacks of severe sternal pain; each wakened her during the night and lasted about 45 minutes. She had a blood pressure of 130/100; the cardiogram showed left axial deviation with flat T in all leads, and a diphasic T in some beats of lead I but not in all. The remaining findings were consistent with a myxœdema heart. Because she had a flat sugar tolerance curve, and because the attacks occurred exclusively through the night, the possibility of hypoglycæmia was considered. Glucose at bedtime was ordered as well as thyroid; unfortunately both were started simultaneously so that it is not possible to say which led to disappearance of the attacks. It is now five years since treatment was instituted; she has had no further attacks, nor has she developed effort angina. Her basal metabolic rate, originally −25 per cent, is now +13 per cent on a dosage of 3 grains daily; she has well-defined upright T waves in leads I and II (amplitude 4 mv. in lead I with a shallow

inverted T III; her blood pressure is 170/95; X-ray shows widening of the root of the aorta and slight enlargement of the left ventricle.

Case 11 had a post-operative myxœdema (basal metabolic rate, —33 per cent) with achlorhydria and anæmia (hæmoglobin 75 per cent, erythrocytes 3·8 million). She had soft heart sounds, left axial deviation with low P and T waves in the cardiogram, and a blood pressure of 155/90. She complained of attacks of precordial pain which she said were usually induced by a sudden noise such as a cough in the ward or the dropping of a plate. The attacks ceased when, in response to treatment with iron, her hæmoglobin rose to 92 per cent. She was then treated with thyroid, and there was no recurrence of pain with doses up to 3 grains daily.

In neither of these cases is there any good evidence of independent heart disease, although in both the blood pressure reading with left axial deviation in the cardiogram raises the question of a possible incipient hypertension; both had "myxœdema T waves" in their original cardiogram. In neither case was there any aggravation of the spasmodic angina when thyroid was given, nor was an effort angina induced by it. In one, the improvement can be attributed to improvement in the blood picture in response to iron. In the other, improvement may have been due either to glucose or to thyroid.

Psychoneurotic Pain.—Although the pain in Case 9 was originally diagnosed as psychoneurotic, it is clear in retrospect that it was really a symptom of Zondek's "abortive myxœdema heart" syndrome. The spasmodic attacks in Case 11 may have been psychoneurotic in view of the conditions by which they were induced, but the rapid response to iron treatment of her anæmia suggested that they were related to the latter. I am not satisfied that I have encountered an example of psychoneurotic pain complicating myxœdema, although it is a possibility which cannot be excluded.

Summary

Several types of anginal pain may occur in myxœdema.

Angina of effort occurs frequently when there is independent heart disease and occasionally with an uncomplicated myxœdema heart. In the presence of independent heart disease, angina is sometimes aggravated, sometimes alleviated, and sometimes unaffected by thyroid therapy. For many patients there is an optimum dose, up to which improvement results but beyond which the pain is aggravated; the optimum dose is often sufficient to procure great improvement in the patient's general condition and to permit of a fair amount of activity; in favourable cases the angina is abolished on the optimum dosage. When a patient with myxœdema and independent heart disease suddenly develops effort angina during thyroid treatment and apart from an increase in dosage, the cause is frequently a small coronary occlusion; caution suggests that the dose should be temporarily reduced or discontinued; but once the stage of convalescence has been reached resumption of therapy does not aggravate the pain, and there seems to be no reason for withholding the benefits of the drug.

A constant ache or pain, aggravated during effort, and tending to be associated with attacks of collapse, occurs in some cases of mild or sub-clinical myxœdema; it is referred to as the *abortive myxœdema heart of Zondek*. It improves with thyroid therapy, but in these cases too there may be an optimum dose. If unrecognized and untreated, the patients may develop a typical clinical myxœdema or a typical angina of effort.

Spasmodic angina occurred in two cases. Both may have had very early hypertension, but neither had any obvious or advanced complicating heart disease. In one, the possibility of hypoglycæmia was considered; the attacks ceased on treatment with thyroid and a dose of glucose at bedtime. In the other, there was a complicating anæmia the attacks ceased when this was treated and before any thyroid was given. In neither case did thyroid aggravate the spasmodic angina nor did it produce an effort angina.

The occurrence of anginal pain in a myxœdematous patient does not contra-indicate the

cautious use of thyroid; only when pain develops in response to an increased dosage is there justification for blaming the drug, and even then it may be tolerated at a later date.

I wish to express my indebtedness to Dr. Angus Scott for access to his records of numerous cases of myxœdema, from among which cases 1, 5, and 11 are recorded; also for much helpful discussion. I have also to thank Dr. Eaton for the metabolic investigations, Dr. Wilson and Dr. McWhirter for the radiology, and those practitioners who have sent information regarding patients unable to attend for re-examination. Finally, Mrs. A. Mather has given invaluable help in tracing a number of the patients.

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Table and Appendix of Case Notes

Case No., Age, and Sex	Clinical Features	Cardiovascular Findings	Cardiogram
1. F. 62	1939, Myxœdema. 1942, "	Myxœdema heart. P.B. 136/80 B.P. 150/100	Normal axis, low P and T. Slight L. axial deviation.
2. F. 68	Myxœdema with hypertension.	Enlarged heart. B.P. 190/106. Apical systolic murmur.	Left axial deviation; low P and T. T I invisible. T IV diphasic.
3. F. 54	Myxœdema with hypertension.	Enlarged heart. B.P. 220/110	Left axial deviation; low T; inverted T III.
4. F. 56	Myxœdema with coronary disease, etc. Hb. 86 per cent.	Slight enlargement left ventricle and calcified plaque in aorta.	Slight left axial deviation. Prominent Q III, no Q II. Low T. Inverted T I.
5. F. 57	Myxœdema with coronary disease. Hb. 48 per cent raised to 60 per cent before thyroid started.	Heart not enlarged, heart sounds soft. B.P. 146/94.	Left axial deviation. Inverted T I and T II, slightly elevated R–T III.
6. F. 56	Mild myxœdema	Left ventricular enlargement. B.P. 130/76.	Left axial deviation; low P and T; inverted P III and T III. Partial block twice.
7. F. 50	Mild myxœdema. Hb. 92 per cent.	Heart enlarged, sounds distant. B.P. 142/86.	Left axial deviation; low P and T; shallow inverted T III. P–R 0·24 sec.
8. F. 54	Mild myxœdema and later menopausal thyrotoxicosis.	Heart enlarged. B.P. 172/92. Apical systolic murmur. Pulse rate 100.	Left axial deviation; low T waves (max. 1·5 mm.).
9. F. 54	1938, no clinical myxœdema, diagnosed "neurosis" *May* 1942, typical myxœdema. B.M.R. −16 per cent. Hb. 120 per cent. *Oct.* 1942. No clinical signs of myxœdema on 1½ gr. thyroid daily. B.M.R. −16 per cent.	Heart not enlarged. B.P. 150/86. Slight general enlargement of heart. B.P. 166/90. Heart not enlarged. B.P. 132/76.	Left axial deviation; T of good amplitude. T waves now lower, otherwise unchanged. Unchanged.
10. F. 50	Myxœdema. B.M.R. −25 per cent.	Heart enlarged. B.P. 130/100	Left axial deviation; low T. Diphasic T in some beats of lead I.
11. F. 51	Myxœdema with anæmia. Hb. 75 per cent.	Heart not enlarged; soft sounds. B.P. 155/88.	Low voltage; slight left axial dev. Flat P and T.

Nature of the Pain and its Relation to Thyroid Treatment.

Case 1. Effort angina appeared after 3 years' treatment, 5 weeks after dose raised from 2 to 3 gr. daily. Pain lessened, not abolished, on return to 2 gr. daily.

Case 2. Sudden onset of effort angina after 3 years on 2 gr. daily. Dose temporarily halved, later restored. Ten months later, pain limited to the gums and felt only if walking against a cold wind. Diphasic T IV three months after onset of pain.

Case 3. Onset of effort angina after 3 months on 4 gr. daily, but not reported and treatment continued; B.P. gradually fell to 180/98; cardiogram unchanged. After 9 months, pain improved, ultimately disappeared, and B.P. rose to 220/110. Observed 4 years; no recurrence of pain even when dose later raised to 6 gr.

Case 4. Effort angina present prior to thyroid therapy. Pain abolished on 3 gr. daily, but returned soon if treatment stopped. X-ray and cardiogram unchanged 3 years later; B.P. 155/105; Hb. 84 per cent; B.M.R. −32 per cent, yet active.

Case 5. Effort angina present prior to thyroid therapy. Three days later while patient confined to bed, severe bursting pains in arms; treatment stopped. Sixteen days later, cardiogram showed right branch bundle block. Treatment resumed after discharge from hospital with 2 gr. thyroid daily. Effort angina unaffected by thyroid.

Case 6. Effort angina present before treatment started. Attended irregularly from 1934 to 1937 for 3 to 4 weeks every 4 to 6 months. Complaint of effort angina on each occasion, and improved while on 2 gr. thyroid daily. 1937–40: various treatments but no thyroid; effort angina persisted. 1940: reduced her activities and myxœdema seems to have improved spontaneously; no pain since; no clinical evidence of myxœdema now, and B.M.R. +5 per cent.

Case 7. Found unconscious when 47; symptoms date from this. Pain starts in l. axilla, radiates to cardiac apex and to sternum; worse when excited or after exertion. Thyroid advised but not given. Three years later, typical effort angina. Cardiogram unchanged, P–R, 0·16 sec.; Hb. 78 per cent; B.M.R. −17 per cent.

Case 8. When 48, loss of hair treated by thyroid, but was intolerant. Menopause when 49 with transient exophthalmos and later palpitation, tachycardia, and loss of weight. Effort angina since then. A thin woman with scanty hair and eyebrows, impalpable thyroid, v. Graefe's sign, tremor, and glycosuria.

Case 9. 1938. First had pain in 1935 while nursing sister who died from heart disease. Pain in bouts lasting a few days; constantly present during attack, but worse after a day's work; felt across præcordium, in left shoulder, and inner side of left arm.

May 1942. Pain constantly present at apex, worse on walking, with tightness in chest; two attacks of collapse. Improves and sometimes free from pain with thyroid in doses up to 3 gr. daily but cannot tolerate 4 gr. daily.

October 1942. Prior to operation, thyroid reduced in error to 1½ gr. daily. Attack of pain and collapse occurred an hour after abdomen was painted with strong iodine; pallor, pulse slow and weak, B.P. 140/90, heart sounds good. Attack lasted 4 hours and next day abdomen showed an intense iodine rash with pustulation.

Case 10. Five attacks of spasmodic nocturnal angina over a period of 9 months prior to therapy. No attacks in 5 years since treatment started with 3 gr. thyroid daily and glucose at night. T waves now good. B.M.R. +13 per cent.

Case 11. Attacks of precordial pain induced by sudden noise, etc.; ceased when Hb. rose to 92 per cent with iron, before thyroid started. No recurrence on thyroid, gr. 3 daily.

COMMON AORTO-PULMONARY TRUNK: A RARE CONGENITAL DEFECT

BY

C. W. CURTIS BAIN AND JOHN PARKINSON

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A lad of eighteen was first seen on May 18, 1942. A congenital heart lesion had been diagnosed when he was a few weeks old, and though he was not then cyanosed at rest, he soon became blue and breathless on exertion, especially in cold weather. He had scarlet fever at the age of ten, but never rheumatism in any form. At the age of twelve, he was too breathless for any but short walks. He was unfit to play any games at school. A change had taken place six months before (October, 1941) when cyanosis became permanent and the dyspnœa more distressing. There had been neither orthopnœa nor œdema; he had never fainted, and he had not lost weight. Pain had started during these last months of increased dyspnœa, and now constituted the greater complaint, though he was no complainer. On exertion it began in the left arm and if severe it affected the right. It was felt across the chest, especially on the left, but not in the back. Rest, especially if with warmth, relieved it, yet it might last 10 to 20 minutes once evoked by exertion. There was a slight occasional cough. was felt on emotion or exertion. It never began at rest. Palpitation

Examination.—He was a pleasant and fairly well-developed youth, with some cyanosis of the skin and moderate clubbing of the fingers and toes. The pulse was 70–80, and regular. The blood pressure was 125/100. A heaving apex beat was felt in the fifth space, two inches outside the nipple line. A long diastolic thrill was felt widely in the apical region, yet there was no thrill at the base. The first sound was snapping internal to the apex, and a thundering diastolic murmur was heard over the whole apical region, up to the fourth rib, though loudest internal to the apex. At the base the murmur was less loud; the basal second sound was just audible. There were no abnormal signs in the lungs or abdomen.

The electrocardiogram (Fig. 1A) showed a small R and a large S in all leads, and an iso-electric T in lead I. Two months later, three days before his death on July 18, 1942, T I was inverted (Fig. 1B).

Cardioscopy showed enlargement of the heart, mainly to the right, but with a single big rounded prominence on the left, in the region of the pulmonary artery and extending upwards to embrace the aortic area so that no aortic knob was visible. The right pulmonary artery was, however, not enlarged. In the right (I) oblique position, a barium swallow showed a combined aorto-pulmonary impression and no particular displacement of the left auricle. Radiographs by Major Peter Kerley are shown in Fig. 2 and 3.

Course. A tentative diagnosis was made of patent ductus arteriosus with aneurysmal dilatation of the pulmonary artery, presumably combined with some other defect. This presumption seemed to preclude operation when this was considered because of the deterioration in his condition as already described. The physical signs by July 14, 1942 had altered as follows. Cyanosis was extreme, though he was not, even now, breathless at rest and could walk slowly in the street. The murmur had become more continuous, but it had not the characteristic variation of a ductus murmur. The liver was palpable and pulsating, but there was no œdema.

Four days later, in the evening black-out, he failed to get a taxi and took the underground

tube to return to his friends in their suburban home. At that station the escalator had ceased working, so he was forced to climb the stairs from the station level to the surface, whereupon he died suddenly. We were allowed to perform a post-mortem examination.

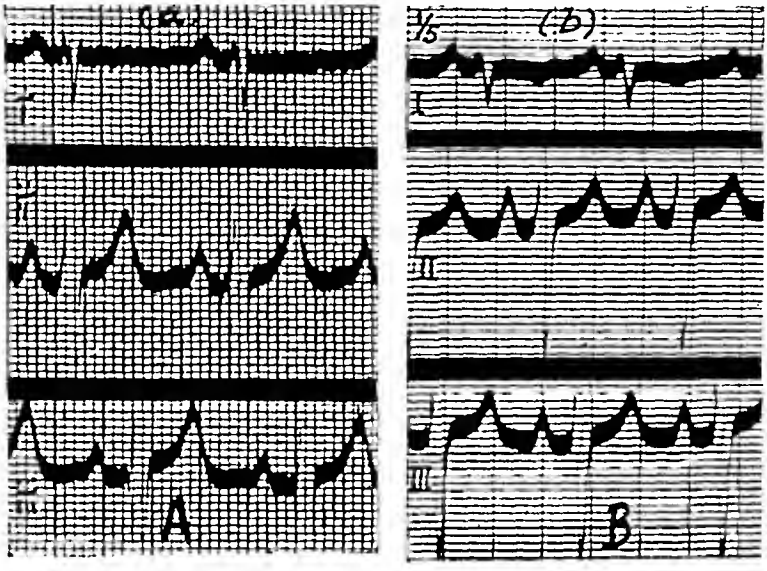

FIG. 1.—Electrocardiograms, (A) taken on May 18, and (B) taken two months later, July 15, 1942.

FIG. 2.—Radiograph (anterior view) showing aortopulmonary sac.

FIG. 3.—Radiograph (right (l) oblique view), with barium in the œsophagus.

NECROPSY REPORT.

A fairly nourished man of average build, with no œdema.

The *pericardium* is normal and the sac contains about 7 ounces of clear fluid.

The *heart* on external examination appears greatly enlarged, chiefly owing to the size

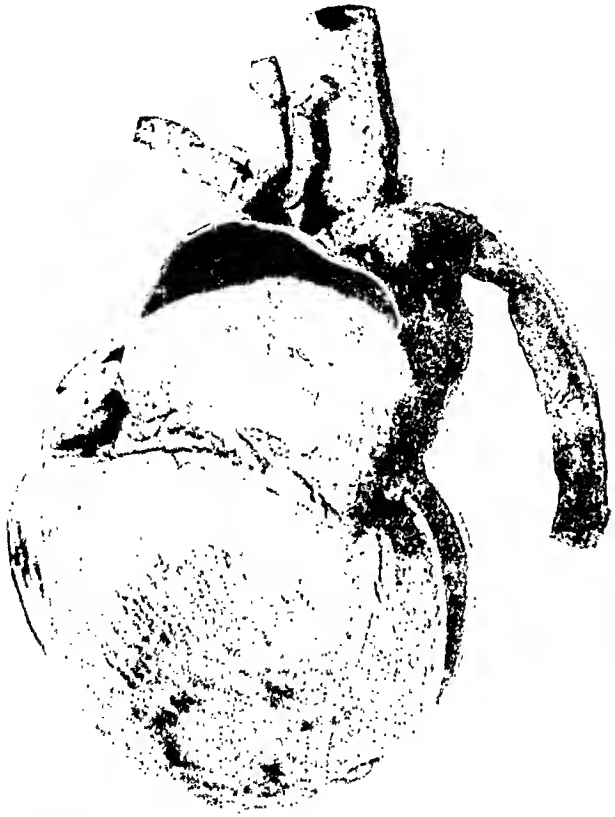

FIG. 4.—Photograph of post-mortem specimen. Anterior external view, showing the ventricles, and the aorto-pulmonary sac, incised.

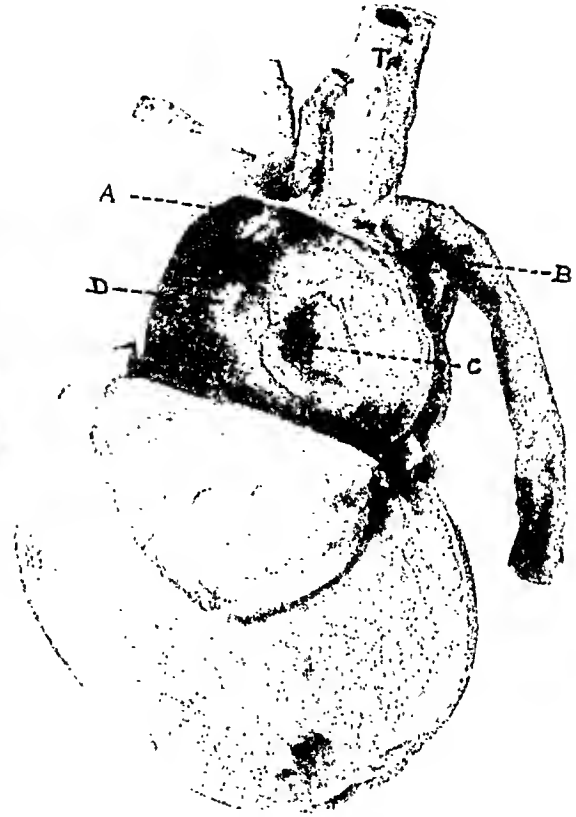

FIG. 5.—Anterior view, showing interior of sac. Of the six orifices, four are here shown, those which lead into:
(A) the brachio-cephalic trunk,
(B) the descending thoracic aorta,
(C) the left pulmonary artery, and
(D) the right pulmonary artery.

FIG. 6.—View from above showing the two remaining orifices into the sac, namely,
(E) the aortic valvular orifice, and
(F) the pulmonary valvular orifice.
The deformity of the cusps is a post-mortem (formalin) change.

of the right ventricle, which forms most of the anterior surface of the ventricles and most of the apex, while the left ventricle forms a small part of the left border and reaches the apex. The conus of the right ventricle seems prominent and the left auricular appendage is well hidden. The right auricular appendage is easily visible on the right.

Above the ventricles is seen a single ovoid *aorto-pulmonary sac*, measuring $8 \times 7 \times 6$ cm. after fixation in formalin (Fig. 4). Externally it looks as if composed of the ascending aorta and a (larger) dilated pulmonary artery. Between these two elements a small vein runs downwards on the anterior outer surface of the sac to the base of the ventricles. The right or aortic element is yellowish—but not so yellow as a normal aorta—and forms about one-third of the total sac as seen externally. The pulmonary artery element is bluish, and forms about two-thirds of the sac. The superior vena cava is normal.

On incising the sac, it proves to be single and undivided, with nothing to suggest any division into aortic and pulmonary stems. The wall of the sac is similar to that of an average aorta and is uniform in thickness (0·125 cm.). The internal surface is smooth throughout, and there is no ante-mortem clot.

Opening into the sac from above downwards, are six apertures (Fig. 5 and 6).

(A) A rounded orifice leading to a common brachio-cephalic trunk which after a course of 1 cm. divides into innominate, left common carotid, and left subclavian arteries.

(B) An oval and rather narrow orifice leading into a smallish descending thoracic aorta with an external diameter of 1·7 cm. in the formalin preparation.

(C) A slightly-funnelled orifice of the left pulmonary artery.

(D) A funnelled orifice of the right pulmonary artery.

(E) The aortic valvular orifice, leading from the left ventricle into the base of the sac. The aortic orifice and cusps are normal, with normally situated orifices of both coronary arteries.

(F) The pulmonary valvular orifice (2·3 cm. diam. after fixation in formalin), leading from the right ventricle into the base of the sac, and separated from the aortic valvular orifice (E) by a wide bridge (1·5 cm. broad) of the aorto-pulmonary saccular wall at its base (or caudal extremity). There is slight cord-like thickening of the middle of the free margins of the otherwise normal cusps of the pulmonary valve.

On opening the heart the right ventricle is seen to be very greatly hypertrophied (1 cm. thick) and slightly dilated. The right auricle is slightly hypertrophied and dilated. There is no dilatation or hypertrophy of left ventricle (1·2 cm. thick) or left auricle. No ante-mortem thrombus is found in the heart or great vessels. The mitral and tricuspid valves are normal.

The *pleuræ* are normal, without adhesions, and each sac contains a few ounces of clear fluid. The *lungs* are moderately congested. The *brain* and the cerebral and cranial vessels are normal. The *liver* is slightly enlarged, very firm and congested. There is great congestion of the hepatic veins, and of the inferior vena cava. The *spleen* is of normal size, firm, and congested.

Summary

A common aorto-pulmonary trunk, as an isolated gross congenital malformation, was found at death in a man of eighteen years, who had always been cyanosed and breathless. Electrocardiograms, radiographs, and pathological details are recorded. The malformation cannot be classified as persistent truncus arteriosus, because there was neither a defect of the interventricular septum, nor any abnormality of the aortic and pulmonary valves.

We wish to thank Dr. J. W. Brown for his valued opinion, Major William Phillips, R.A.M.C., for clinical help, and Major Peter Kerley, R.A.M.C., for the radiographic investigation. To Dr. W. W. Woods, Assistant Director of the Pathological Institute of the London Hospital, we are much indebted for amplifying and completing the necropsy report.

FATAL CORONARY THROMBOSIS IN A MAN AGED TWENTY-TWO

BY

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From the Laboratory, R.N. Hospital, Haslar, and the Bernhard Baron Institute of Pathology, the London Hospital

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We have been able to find only two cases of coronary thrombosis in young adults published in this country (Fernando, 1935, and Blaze, 1937). Both were reported from Ceylon, and the following case of coronary thrombosis in a man aged twenty-two in this country is therefore thought worthy of record.

CASE REPORT

C. A. S., a leading air mechanic, died suddenly at the age of 22 years and 4 months. He was dead before medical attention could be given, and the following history was obtained from relatives, friends, and Service medical records.

There was no family history of circulatory or other relevant disease. Three of his grandparents died in old age; his fourth grandparent, both his parents, and his two siblings were alive and well.

Apart from measles in childhood, influenza five years before his death, and occasional common colds for which he required no medical attention, he had had no illness. He had always led an active life, swimming and cycling and playing cricket and football. He seldom drank alcohol and smoked about ten cigarettes a day. He was a clerk in civilian life and joined the Navy over three years before his death. During this period his medical records show that he served in several different shore establishments without illness of any kind, and that he was always found fit at routine medical examinations.

A comrade who had been his close companion in the Navy for the last two years of his life supplied the following details. C. A. S. appeared to be normal and healthy in every way and never complained of pain, breathlessness, or any other symptoms. On the evening before his death they had a meal ashore together and went to bed at their usual time. Nothing untoward happened during the night. They got up as usual at 6.45 the next morning and the patient then appeared quite normal. Half an hour later he complained of "feeling queer," but carried on working (bed-making). He did not appear to be particularly ill, but about an hour after first complaining he suddenly collapsed on the floor. He was placed on his bed, where it was noticed that his respirations were slow and sighing and that he was very pale. Breathing stopped a few minutes later, and when he was examined by a doctor shortly afterwards he was found to be dead.

SUMMARY OF NECROPSY AND OF MICROSCOPICAL FINDINGS

A well-nourished young man of good physique, with no external evidence of injury or disease. Left coronary artery (0·9 cm. long) normal. Lumen of first 4·5 cm. of anterior descending branch of left coronary occluded by firm, grey, completely organized, canalized

thrombus, fused with a slightly fatty atheromatous hypertrophied intima. Remainder of anterior descending branch normal except for slight hypertrophy of intima. Considerable stenosis by atheroma, and occlusion by organizing thrombus of first 0·5 cm. of circumflex branch of left coronary artery, and slight stenosis by atheroma, 1 cm. from its origin. Circumflex branch abnormally short, ending as the left marginal artery. Numerous minute flecks of fatty atheroma and one larger atheromatous area (0·4×0·3 cm.) in right coronary artery, without stenosis of lumen. No recent coronary thrombosis found. Coronary sinus and its tributaries normal. Numerous, irregularly branched, white areas of isehæmic fibrosis of myocardium in middle third of interventricular septum, the largest being 1×0·4 cm.; few in lower third; none elsewhere in myocardium. No recent infaretion of myocardium detected. No enlargement of heart (weight 12 oz.). Pericardium and cardiac valves normal. Numerous very small flecks of fatty atheroma in first 2 cm. of aorta, a few in aortic arch and a few, accompanied by sparse faint streaks of fatty atheroma, in descending aorta. Congestion of kidneys. Slight congestion of liver. One pint of semi-digested food in stomach. No abnormality found in brain, mouth, air passages, lungs, or any other organ.

Microscopical Description. In sections of the anterior descending branch at the upper end of the occluded area, the lumen is filled with a tissue composed of fibroblasts, collagen fibres, a few macrophages containing pigment and giving a positive reaction for iron, numerous capillaries and numerous vessels with walls composed of thick layers of involuntary muscle fibres and elastic fibres; most of these well-developed vessels lie near the intima and have very narrow lumina. In sections 2 cm. further down the artery the canalizing vessels have wider lumina and their walls contain less muscle but abundant elastic fibres. In both sets of sections the intima is hypertrophied, having developed a thickened longitudinal musculo-elastic layer between the elastic lamella and the elastic stripe, as well as a hyperplastic elastic layer internal to the latter (Fig. 1). Frozen sections stained with Sudan III show very slight focal fatty atheroma in the hypertrophied intima. The media of the anterior descend-

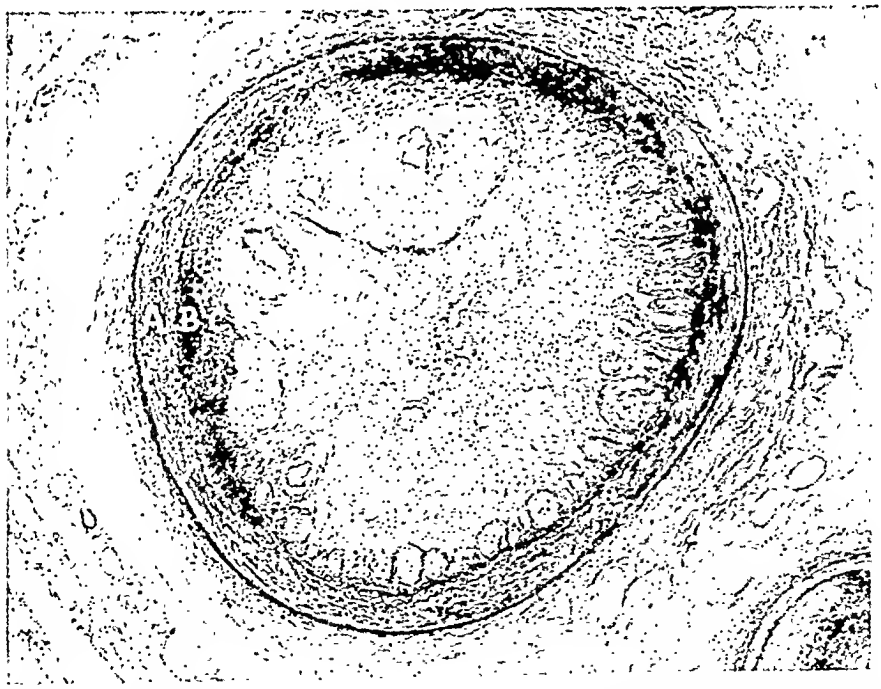

FIG. 1.—Upper part of anterior descending branch, occluded by canalized organized thrombus. A=media. B=longitudinal musculo-elastic layer of intima. C=Hyperplastic elastic layer of intima. Weigert's fuchselin and neutral red. ×32.

The section has been overstained in Weigert's fuchselin to make the elastic fibres in the new vessels of the organized thrombus more distinct in the photo; this overstaining has the disadvantage of making the division between layers B and C less distinct, although this division is absolutely clear when the section is examined with the microscope.

ing branch is normal except that it is unusually rich in elastic fibres. The adventitia is normal except that the small vessels in and outside it are dilated. The neighbouring smaller and larger branches of the artery are normal except that in one of the largest there is slight fibro-musculo-elastic hypertrophy of the intima. The lower half of the anterior descending branch is normal except for slight hypertrophy of the intima, consisting chiefly of proliferated elastic fibres. There is a considerable amount of elastic in its media. Its branches are normal. Two transverse pieces were taken from the first 0·5 cm. of the circumflex branch for paraffin embedding, and one piece for frozen sections. Areas of atheromatous intima, several times thicker than the normal media, bulge into the lumen; these areas have an inconspicuous longitudinal musculo-elastic layer, and consist mainly of a greatly thickened hyperplastic layer which is composed of abundant delicate elastic and collagen fibres and numerous spindle and polygonal macrophages full of fat. The lumen is occupied by a central area of fibrin with a few leucocytes and red blood corpuscles and a broad peripheral zone of delicate connective tissue composed mainly of fibroblasts and capillaries and containing very few slender collagen fibres and no pigment macrophages. In the adventitia and extra-adventitial connective tissue there is dilatation of capillaries and very slight infiltration with lymphocytes, but nowhere is there any suggestion of acute or chronic arteritis. In a similar series of sections of the circumflex branch, taken 1 cm. from its origin, there is a slightly lesser degree of atheroma and no other abnormality. No hæmorrhage and no capillaries were seen in the intima above and at the sides of the areas of atheroma in any of the coronary arteries. In the large pieces of interventricular septum included in these sections there is much old ischæmic destruction of myocardium, showing as numerous areas of muscle replaced by dense fibrous tissue which is remarkably rich in elastic fibres. There is no fatty degeneration of the myocardium to be seen in frozen sections of the interventricular septum stained with Sudan III. The largest coronary branch in the myocardium in these sections has its lumen obliterated by a tissue similar to that described in the occluded part of the anterior descending branch; this tissue is fused with the hypertrophied intima, which consists chiefly of elastic fibres.

Congestion is conspicuous in sections of the kidney, but there is no other abnormality. Congestion is less obvious in the liver.

Discussion

The incidence of coronary thrombosis before the fifth decade varies according to different authors. White and Mudd (1927) found 3 per cent of 418 cases under 40; Conner and Holt (quoted by Reitman *et al.*, 1942) in a series of 287 cases found 8 per cent under 40 and 1 per cent under 30. Durant, 1937, in his 114 cases of proved coronary thrombosis reported 7 (6 per cent) under the age of 35, only 1 of which was under 30.

Scott (1938) was able to collect a total of 208 cases of coronary thrombosis in patients under 40; of these only 28 were aged 30 or less. Reitman *et al.* (1942), found 34 reported cases below 30, and 4 below 20 years of age, among their total collection of 221 cases under 40.

Although arteriosclerosis has been found in children as young as two years (Stolkind, 1928) and cases of coronary calcification and thrombosis have been reported in infancy; the pathogenesis in these appears to be little related to the accident occurring in later life; thus Brown and Richter (1941) suspect some alteration in the calcium and phosphorus metabolism, and in van Crevald's (1941) case of coronary thrombosis in a girl 7 weeks old, the disease appeared to be related to the use of drugs by the allergic mother.

Apart from infancy, the youngest reported case of coronary thrombosis appears to be at the age of 12 (Dreschfeld and Benda, quoted by Smith and Bartels, 1932). Sprague and Orgaine (1935) describe two cases at 15 and 16 years, proved at necropsy. In the remainder of the published cases of coronary thrombosis in young adults the condition occurs with increasing frequency from the age of 18 upwards.

Coronary thrombosis is so commonly associated with men in their fifties or sixties that its occurrence in young adults might be thought to differ in some essential way from the typical case in later life. Syphilitic aortitis, for example, is sometimes considered a relatively frequent cause under the age of 40; but in the cases reported under the age of 30 it appears to play no part. Since Barron and Linenthal (1929) described thrombo-angiitis obliterans as a cause of coronary thrombosis, it might be expected that this disease would account for at least some of the cases of coronary thrombosis in young adults, but again there is no reported evidence of this.

Herapath and Perry (1930) have reported a family remarkable for the early age at which there were sudden deaths of four different members, and this is probably an important factor

in the occurrence of cases early in life. The father died suddenly of heart disease when 42. There were nine children, of whom three sons died suddenly from heart disease, each at an early age. The second son died at 30. The fifth son, aged 32, was taken ill when playing football and died within an hour, his heart showing gross atheromatous changes in the coronary arteries. The eldest son, then aged 39, was already complaining of a tight feeling in his chest when he hurried or took any exercise. Four years later the attacks were worse, and were associated with severe anginal pain even on quiet walking. The heart was not enlarged, and the cardiogram, which had been normal two years before, now showed inversion of the T waves in leads II and III. A month later he fell dead while getting into a tram. There were atheromatous changes in the thoracic and abdominal aorta with ulceration and some calcification, the media showing replacement fibrosis and the intima showing extensive fatty degeneration. The coronary arteries were hard and thickened, and after injection showed the increase of vascularity corresponding to an extreme degree of the "age change" described by Gross as occurring in a man of over sixty.

The following eleven cases of coronary thrombosis at the age of 30 and under have been abstracted; in the other published cases either the data given are insufficient for comparative purposes or the original papers were not available.

1. Fernando (1935) reported the case of an athletic male Cingalese, aged 24, who had attacks of anginal pain with dyspnœa, occurring first while in bed. An electrocardiogram (EC.) confirmed the diagnosis of coronary thrombosis. The patient was discharged from hospital after two months. Wassermann reaction negative. No previous illness. Mother died of heart attack when 45.

2. Durant (1937) reported the case of a male Jewish student, aged 23, who had three attacks of substernal pain with dyspnœa before admission to hospital. EC. confirmed anterior cardiac infarct. Kahn negative. No relevant family history or previous illness.

3. Blaze (1937) reported a Tamil manual labourer, aged 23, who collapsed on his way to work with symptoms of coronary artery occlusion. He died shortly afterwards and at necropsy an ante-mortem thrombus was found attached to the wall of the beginning of the descending branch of the left coronary artery. Both coronary arteries showed atheromatous plaques. No relevant past history was obtained and family history was not noted.

4. Franklin's (1938) case was an American male, aged 30, who two months before investigation had a sudden attack of severe chest pain lasting two days, and subsequent attacks of less severity. He was a heavy drinker and smoked 20 to 40 cigarettes a day, but had no previous illness except ichthyosis. His mother died, aged 54, of high blood pressure. Kahn negative. EC. was suggestive of myocardial infarction. He gradually improved.

5. Halbersleben (1938) reported the case of a 28 year old American housewife who developed symptoms of coronary artery occlusion while sitting at table. She died five days later, and at necropsy the right coronary artery was found to be occluded by thrombus. Both coronary arteries showed atherosclerotic thickening, and there were extensive areas of infarct necrosis in the myocardium of the left ventricle. She also had a leukæmia, but the white blood count was only 32,000 per c.mm. and the thrombus was not one of white cells. She had a normal pregnancy at the age of 26. There was no relevant previous illness or family history.

6. Scott's (1938) patient was a cost accountant, aged 27. He had presternal pain of some hours duration seven days prior to investigation. EC. showed coronary occlusion of T III type. He gradually improved. He had chorea at 7, but no other previous illness. Wassermann negative. He smoked 15 to 20 cigarettes a day, and seldom drank alcohol. His father died of apoplexy when 63; one of his mother's sisters died of diabetes when 59 years old.

7. Goodson and Willius (1939) reported three cases of coronary thrombosis under the age of 30, but give details of only one. This was a housewife, aged 22, in the third month of her first pregnancy. She fell from a low porch and sustained a head injury, remaining unconscious until she died 16 hours later. The necropsy findings were an acute infarct of the posterior wall of the right ventricle and a linear infarct of the central portion of the interventricular septum extending from the base to the apex. There was no atherosclerosis of the coronary arteries according to the authors; since petechial hæmorrhages were found in the cortex they were uncertain whether the fall was occasioned by the severe pain of coronary thrombosis or whether the coronary thrombosis occurred as a result of the fall.

8. Ferguson and Lockwood (1939) published the case of an American truck driver, aged 26, who was afflicted with substernal and epigastric pain of sudden onset, increasing to maximum severity in 24 hours, radiating to the left shoulder and arm. EC. showed progressive myocardial damage but were not in themselves diagnostic of coronary occlusion; yet a pericardial rub and inversion of T I indicated a lesion in the anterior and apical region. Wassermann reaction negative. He recovered and was alive and well after six months. He had no previous illness but had used tobacco excessively for years (no amount stated). His father died, aged 40, of cardiovascular disease.

9. Dawber's (1941) case was a man, aged 21, in a Marine hospital who developed symptoms of coronary occlusion, following two 6-hour periods of hyperthermy at 106° F. for chronic gonorrhœal urethritis. EC. confirmed, showing an anterior infarction. Repeated serological tests for syphilis were negative. The patient survived this attack. He had no other disease. No note of family history is made.

10. Macdonald (1941) reported coronary thrombosis, in a male of 21, which proved fatal about a year later, in the third attack. No family or previous history is noted. The original attack started while he was walking home after a game of softball, during which he was struck on the chest. The anatomic diagnosis at necropsy was atherosclerosis, stenosis, and thrombosis of the coronary arteries (old thrombosis of the left with recanalization, and recent thrombosis of the right artery); and infarcts of the heart (healed and recent).

11. Reitman *et al.* (1942) published a case of coronary thrombosis in a student, aged 20, who since the age of 9 had diabetes, which was controlled by diet and protamine insulin at the time of the attack. Past history was otherwise normal. No family history noted. Precordial pressure and dyspnœa on slight exertion began two days after the patient had gone swimming and had to swim some distance to reach the shore. The eyegrounds showed early tortuosity of the vessels with moderate atherosclerotic changes. EC. showed evidence of acute myocardial infarction involving the posterior surface of the left ventricle. The authors ascribe the early onset of coronary thrombosis in this case to hypercholesterolæmia; the blood cholesterol was 350 mg. per 100 c.c. The patient survived this attack.

Analysing the above eleven cases along with the one here reported we may observe that in twelve cases of coronary thrombosis between the ages of 20 and 30:

Ten patients were male and two female (in 27 reported cases of coronary thrombosis under 30 in which the sex was stated, there were only 4 females).

There appeared to be no special predilection for race or occupation.

Four died in the first attack; the remaining eight survived for some months at least.

There was a rheumatic history in only one (Case 6).

Syphilis was not once the cause.

Of seven whose family history is noted, four had evidence of familial " defective tubing."

Atheroma or atherosclerosis was the lesion found in all four cases which came to necropsy and are adequately described. Goodson and Willius' case must be omitted for lack of microscopical data. Scott (1938), referring to his collection of 208 cases of coronary thrombosis under 40, states: " Arteriosclerosis is the pathologic lesion invariably found in all of the cases referred to in this paper that have come to autopsy."

Raised blood pressure was present in only one of the twelve cases (Halbersleben's case; blood pressure about 150/85 for years). Signs of arterial disease, apart from those of coronary occlusion, were absent in these cases.

Summary and Conclusions

A case of sudden unexpected death from coronary thrombosis and ischæmic fibrosis of the myocardium is described in a man of twenty-two. Thrombosis had occurred in the anterior descending branch so long before death that the thrombus was completely organized and contained vessels with musculo-elastic walls. There was a more recent incompletely organized thrombus in the circumflex branch. The examination revealed neither a thrombus that had formed immediately before death nor a recent myocardial infarct. The only disease

found in the coronary arteries predisposing to thrombosis was atheroma. There was no history of any illness before the attack, which started about one hour before death.

2. The reported cases of coronary thrombosis in young adults are reviewed. The condition in young adults is very similar to the typical case in later life except that raised blood pressure has rarely been noted. The pathological lesion found in the cases that have come to necropsy is atheroma (atherosclerosis) of the coronary arteries, the anterior descending branch of the left coronary being most frequently the site of thrombosis.

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SYPHILITIC ANGINA PECTORIS

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The first description of an actual case of syphilitic angina pectoris has been credited to Morgagni (1761). It concerned a woman, aged 42, who had anguish in the upper part of the chest, with difficulty in breathing and numbness of the left arm, provoked by exertion and promptly relieved by rest; while on a journey from Venice, she died suddenly in a paroxysm. At necropsy, the arch of the aorta was dilated, its inner surface irregular and ossified, and the valves indurated. Following Heberden's account of angina pectoris, Blackall (1814) and, later, Corrigan (1838) reported its association with disease of the aorta, which, at that time, had not been connected with syphilis. After syphilitic aortitis had been identified and separated from atheroma (Welch, 1876), its relation to angina pectoris became recognized, especially by Allbutt. His aortic theory, though no longer entertained in respect of angina pectoris in general, has never been entirely abandoned in the case of syphilitic aortitis.

Thus, Herrick (1931), in subscribing to the coronary theory, did not deny the possibility of an aortic angina which "lacks the earmarks of the typical form." Coombs (1932) remarked that certain features of syphilitic anginal pain were suggestive of a periaortic origin. Stadler (1932) found the distinction between aortalgia and mild angina pectoris difficult. This conception of an atypical or pseudo-angina of aortic origin is still current in descriptions of the symptoms of syphilitic aortitis. It was, of course, opposed by Allbutt (1915), who accused contemporary writers of withholding the diagnosis of angina pectoris at pleasure whenever the coronaries proved to be intact: "Call no man anginous until he be dead, and not even then unless he has played the game."

In investigating syphilitic anginal pain, we have paid special attention to the occurrence of any peculiar or atypical features that might be interpreted in terms of an aortalgia. In order to approach the problem of pathogenesis without bias, we have included in this inquiry all cases of paroxysmal pain the chest of anginoid type occurring in syphilitic subjects, without reference to the physical signs. Non-paroxysmal pain has been excluded; we believe that, in syphilitic cases, it can usually be attributed to pressure from a dilated aorta, and need not be confused with angina pectoris. The presence of aneurysm sometimes gave rise to difficulty in diagnosis. Osler (1906) first drew attention to the importance of angina pectoris as an early symptom of aortic aneurysm, and Mackenzie (1923) also accepted the association as common. More recently, Campbell (1936) has stated that 15 per cent of all cases of thoracic aneurysm are subject to anginal pain. We have, therefore, not excluded cases of aneurysm from consideration except when obvious pressure symptoms or signs rendered the interpretation of pain difficult.

CLINICAL MATERIAL

The records of 103 patients with evidence of syphilitic infection and subject to anginal pain, in the sense defined, have been analysed. They were seen by one of us in hospital and practice, mostly during the last ten years, and details of the pain were recorded personally. It is not suggested that syphilis was invariably a causative factor, for atheromatous coronary

disease is always probable in those of appropriate age, yet aortitis cannot be excluded at any age in a syphilitic subject. In such a series of cases it should be possible to identify the essential characteristics, if any, of syphilitic anginal pain.

Evidence of Syphilis. One or more of the following criteria of syphilitic infection was present in every case.

(1) A history of primary or secondary syphilis, or of treatment for it.
(2) A positive Wassermann (W.R.) or, occasionally, Kahn reaction.
(3) Unquestionable syphilitic lesions other than cardiovascular.
(4) Aortic incompetence with a typical X-ray picture of syphilitic aortitis, that was not otherwise explicable.

A positive W.R. (or Kahn in a few cases) was recorded at some stage in 96 cases; in 9 of these, negative reactions were obtained later, after treatment. In the 7 cases without a positive W.R., two gave a history of syphilis and had typical dilatation of the aorta without hypertension, 4 had aortic incompetence with syphilitic lesions elsewhere, and 1 had aortic incompetence with a dilated aorta suggesting aortitis.

There was a history of primary or secondary syphilis in 31 cases, in 29 of which the date of infection was recorded. The interval between infection and the onset of anginal pain varied between 7 and 44 years, the average being 24 years; in 11 cases it was less than 20 years and in 18 cases 20 years or longer.

Age. The age at onset of anginal pain in these 103 cases and, for comparison, that in a series of 540 unselected cases of angina pectoris seen by one of us, is given in Table I.

TABLE I

AGE INCIDENCE OF SYPHILITIC ANGINA PECTORIS COMPARED WITH THAT IN A SERIES OF UNSELECTED CASES

Age at onset of pain	(PERCENTAGES)				
	30–39	40–49	50–59	60–69	Over 70
Syphilitic angina—103 cases	10	32	30	28	0
Unselected angina—540 cases	3	18	37	32	10

In syphilitic subjects angina started most frequently in the forties, but almost as often in the fifties or sixties. In Gallavardin's (1938) 252 syphilitic cases, the onset of pain was most frequent in the fifties, though fairly evenly distributed between the ages of 40 and 69. The importance of syphilis as the cause of angina below the age of 40 has rightly been emphasized, but it must not be overlooked that syphilitic angina is actually more frequent after than before 50. Several patients in this series, with aortic incompetence, are still alive in the region of 70 years of age.

Sex. There were 80 men and 23 women, giving a sex ratio of 3·5 males to 1 female, which corresponds to the sex ratio in angina pectoris as a whole as given in recent statistics (White and Bland, 1931; Gallavardin, 1938; and Bedford, 1936).

Aortic Incompetence. This was present in 67 cases (65 per cent); occasionally it developed while the patient was under observation and subsequent to the onset of anginal pain. The incidence of aortic incompetence was 100 per cent below the age of 40, 70 per cent between 40 and 50, 47 per cent between 50 and 60, and 65 per cent over 60 years. Gallavardin found aortic incompetence in only 32 per cent of his syphilitic anginous patients. In comparison, the incidence of aortic incompetence in angina pectoris as a whole was 4·8 per cent in our 540 cases, and 5·5 per cent in Gallavardin's series.

Aortic Dilatation. The results of X-ray examination were recorded as follows:

Aorta normal	36 cases
Unfolding of aorta (not typical of syphilis)	19 ,,
General dilatation	22 ,,
Dilatation mainly of ascending part	11 ,,
Aneurysm	7 ,,
X-ray not recorded	8 ,,
	103 ,,

etence developed terminally and subsequent to the onset of anginal pain—the aorta appeared bsolutely normal in the radiograph (Fig. 1); yet necropsy disclosed generalized syphilitic

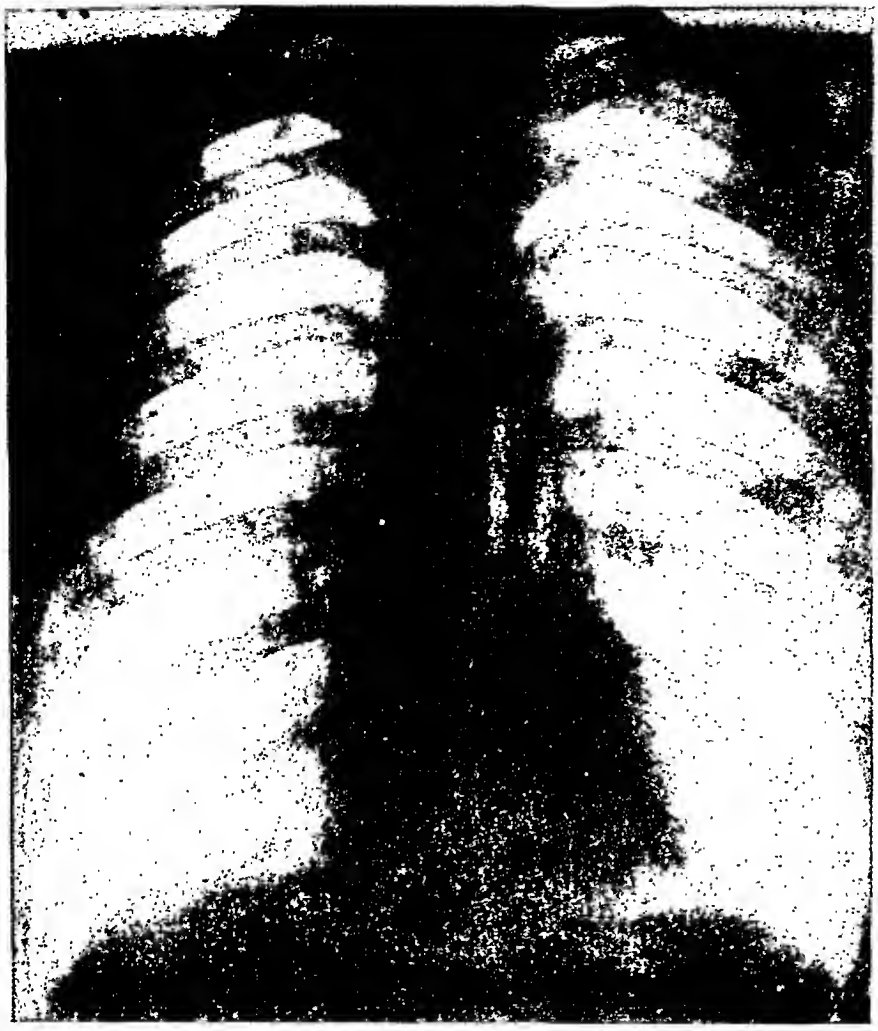

FIG. 1.—Radiograph in Case 45, showing normal appearance of heart and aorta. Necropsy showed severe syphilitic aortitis with stenosis of both coronary ostia.

aortitis without appreciable dilatation, and severe stenosis of both coronary ostia. Absence of aortic dilatation should not exclude a syphilitic ætiology in any case of angina pectoris.

Cardiac Enlargement. The heart, judged by X-rays in all but 8 cases, was normal in size in 20 and enlarged in 83 cases ; in 48 the degree of enlargement was slight. Stenosis of the coronary ostia tends to limit the process of cardiac hypertrophy in aortic incompetence, and this may explain why gross enlargement was not more common.

Blood Pressure. Normal standards of blood pressure are scarcely applicable to aortic incompetence, in which a relatively high systolic and low diastolic pressure represent the effect of cardiac hypertrophy combined with vaso-dilatation. Twenty-six patients (25 per cent) were regarded as having some degree of essential hypertension because of a systolic pressure of at least 200 mm. or a diastolic of at least 100 mm., or both. Thirteen patients had systolic pressure of 170–200 mm. with normal or low diastolic pressures, and this was regarded as the effect of aortic incompetence. In the remainder, pressures were below these

levels. Thus, hypertension is somewhat less frequent in syphilitic than in non-syphilitic angina pectoris.

Electrocardiogram. Records were obtained in 94 cases. They were normal in 37 and abnormal—or became abnormal—in 57 cases. Significant T wave abnormalities occurred in 47, bundle branch block in 5, significant notching of QRS in 18, and 4 showed A-V block of some degree. Transient R–T changes were recorded in the course of severe anginal episodes in 5 cases. Of 12 cases with a terminal status anginosus or stenosis of the coronary ostia at necropsy, the cardiogram was abnormal in 10; bundle branch block occurred in 3, T I inversion in 2, T II and T III inversion in 4, and T inversion in all leads in 1 case. In Case 45, dying in a status anginosus, with severe stenosis of both coronary ostia at necropsy, the curve was normal within a few days of death. In only 2 of these cases was significant R–T deviation recorded; once it was of opposite and once of similar direction to the T waves. The reciprocal R–T and T changes characteristic of myocardial infarction are not usually observed in ostial obstruction. This was also the experience of Muijden and Scherf (1934), of Levy (1936), and of Zimmermann-Meinzigen (1936).

Site of the Pain. It is often stated that the pain of syphilitic aortitis is unusual or atypical in its distribution in comparison with that of angina pectoris proper (Reid, 1930; Coombs, 1930). In the majority of our syphilitic cases the pain was either central or extended horizontally and more or less symetrically across the chest; its level was approximately mid-sternal in 55 cases and in the remainder at the upper or lower thirds of the sternum with almost equal frequency. Pain often spread to the neck or throat (25 cases), to the back (18 cases), and to the shoulders, axillæ, and arms. It affected both arms in 38 cases, the left only in 19, and the right only in 2; this applies to the more severe attacks and not to milder ones in which pain was more confined.

In 7 cases pain started in the left chest and spread to the sternum, in 2 it started posteriorly in the interscapular region, and in 4 in the arms. In only 7 cases could the pain be described as eccentric; in 4 of these it was situated in the left chest and in 3 in the right chest. Such an eccentric distribution is found in a similar proportion of cases of non-syphilitic angina pectoris.

The traditional term *substernal* describes appropriately enough the brief oppression or tightness in the chest on effort which is quickly relieved by halting, but it is an inadequate description of the distribution of severe or prolonged anginal pain, for example in coronary thrombosis or in the nocturnal attacks of syphilitic aortitis. In the present cases, pain was often widespread and involved the spine, neck, or shoulders, but to describe it as atypical or unusual would be unwarranted.

Clinical Varieties of Anginal Pain

(1) *Angina of Effort.* There were 76 patients who were subject to fairly typical anginal pain on exertion, relieved by halting. This was sometimes more severe and more lasting than the usual effort pain. In 13, pain provoked by effort persisted in some degree for 5 to 30 minutes, but it was almost always amenable to nitrites when prescribed. Pain that subsides slowly has been described as characteristic of aortitis (Barrie, 1912; Laubry *et al.*, 1925; and Reid, 1930). Yet Heberden, in describing angina pectoris, wrote: "After it has continued a year or more, it will not cease as instantaneously upon standing still." The following example may be cited.

Case 75. Male, aged 56, first seen August 1934. Syphilis denied. For 2 years subject to pain across chest at mid-sternal level, extending into both arms, provoked by effort and persisting sometimes for as long as an hour. Recently, onset of nocturnal attacks of pain lasting up to an hour, with palpitation and dyspnœa, relieved by nitrites.

Examination. Pulse, regular and collapsing. Arteries, thickened. B.P., 200/70. Aortic diastolic murmur; gallop rhythm at apex. X-ray: slight enlargement of heart and widening of aorta; no signs of congestive failure. EC., normal. W.R., positive.

Course. After rest and mercurial treatment, improved but liable to effort pain. In October 1936, pain more frequent with severe nocturnal attacks, and dyspnœic paroxysms. In August 1937, in hospital with spontaneous anginal attacks accompanied by paroxysmal dyspnœa. EC., bundle-branch block. Died, with increasing pulmonary œdema.

Necropsy. Great hypertrophy of left ventricle and dilatation of right. Gross syphilitic aortitis and deformity of aortic cusps. Right coronary orifice occluded and left orifice stenosed. Coronary trunks normal. Bilateral hydrothorax and pulmonary œdema.

(2) *Angina apart from Effort.* Paroxysmal pain unrelated to effort, either nocturnal or diurnal, occurred in 64 cases, 37 of which also had effort pain. Of the 27 patients without effort pain, 8 were considered to be cases of coronary thrombosis probably associated with atheroma. It is evident that spontaneous and especially nocturnal anginal pain is far commoner in syphilitic than in non-syphilitic anginous subjects. As this kind of pain has been so often described as characteristic of aortitis, as opposed to cardiac ischæmia, we shall consider it in detail under the following headings.

(*a*) Nocturnal angina.
(*b*) Spontaneous diurnal angina.
(*c*) Angina associated with paroxysmal dyspnœa (paradyspnœic angina).
(*d*) Syphilitic status anginosus.
(*e*) Cardiac infarction syndrome.

(*a*) *Nocturnal Angina Pectoris.* Forty-four patients (43 per cent) were subject to nocturnal anginal attacks. If the pain occurred in the early hours of sleep, it was apt to recur once or more before morning; but in some patients it occurred only in the later hours. Occasionally it was described as continuing on and off all night. Pain tended to be severe and persistent, lasting 5 to 30 minutes or even longer unless relieved by nitrites. Patients tend, however, to over-estimate its duration. Some experienced a remarkable predominance of nocturnal attacks which occurred from the start and continued over periods of years. As Gallavardin puts it, these martyrs of the night may be little troubled in the daytime, especially if they avoid effort.

Nitrites almost invariably gave relief and once prescribed were apt to be consumed in extraordinary quantities. An opiate or other sedative at bedtime was often effective in preventing nocturnal pain, and a late or heavy evening meal always aggravated it. Patients with nocturnal angina seem particularly sensitive to a full stomach. The influence of posture is evident in many patients. Some of them experienced pain when lying down, even if awake and in the daytime, whereas sitting upright, standing, or walking about usually afforded some relief. A return to the horizontal posture favoured a recurrence of pain and recourse to sleeping in a chair was occasionally necessary. These repetitive nocturnal paroxysms were described by the earliest writers on angina, for example, Heberden (1802), Parry (1799) and Black (1819). Black's four patients, among the earliest in which coronary disease was demonstrated at necropsy, all had frequent nocturnal attacks and one patient used to sit up on a chair to " baffle the paroxysms."

Palpitation during the attack was a common complaint and tachycardia was frequently confirmed by observation. Blood pressure readings during nocturnal pain were scanty, but a rise of pressure was recorded in several cases. We are satisfied that paroxysmal dyspnœa is not an essential or usual accompaniment of nocturnal pain, as French writers—excepting Gallavardin—have assumed. Cases in which this combination did occur are separately considered.

In a series of 200 unselected cases of angina pectoris, 23 per cent were subject to nocturnal pain compared with 43 per cent in the syphilitic series. The frequency of nocturnal attacks in syphilis has been insufficiently recognized though it has not altogether escaped notice, for example, by Willius (1936) and Oille (1937); it is easily confirmed by reference to published case records such as those of Mackenzie (1923), Osler (1897) and Gallavardin (1925). Aortic

incompetence is the rule and occurred in 77 per cent of our cases with nocturnal pain. The following example is briefly cited.

Case 79. Man, aged 64, first seen September 1926, while under treatment for tertiary syphilitic lesions of mouth. Started attacks of severe mid-sternal pain radiating to spine, unrelated to effort and usually nocturnal.

Examination. Slight enlargement of heart and dilatation of ascending aorta (X-ray). Accentuated aortic second sound; no aortic incompetence. B.P., 150/100. EC., left axis deviation; P–R prolonged, QRS and T normal.

Course. Following rest and anti-syphilitic treatment free from pain for over 2 years, when it recurred. Attacks nocturnal or provoked by lying flat and relieved by sitting up. Became short-winded, signs of aortic incompetence were noticed, and congestive failure soon followed. Improved with treatment for heart failure. In 1934 in hospital with further congestive failure and hydrothorax. B.P. 210/80. Died at home in January 1937, 11 years after the onset of anginal pain.

(*b*) *Spontaneous Diurnal Anginal Pain.* Pain apart from effort during the daytime occurred in 22 cases, half of which were also subject to effort pain and most to nocturnal pain. Such factors as emotion, meals, cold, etc., were often operative. The effect of posture was also mentioned by some patients in whom reclining, stooping, or bending might precipitate pain. The attacks tended to be severe and prolonged and were sometimes accompanied by sweating and palpitation, but were amenable to nitrites when available. Perhaps the most remarkable feature in these syphilitic patients was the period of time—even years—over which severe and prolonged anginal pain occurred without objective signs of deterioration of the heart or failure appearing. Sometimes there were intervals of relative freedom of even remissions.

(*c*) *Paradyspnœic Anginal Pain.* In the past, cardiac asthma was often confused with angina pectoris and even to-day this confusion persists in descriptions of so-called angina of decubitus. Acute pulmonary œdema may start with a feeling of oppression in the chest due to pulmonary engorgement, and this has undoubtedly passed as angina of decubitus. Gallavardin (1933) refers to this sense of oppression as paradyspnœic angor, but does not confuse it with angina pectoris. Admitting occasional difficulty in differentiating between the two, there is no doubt that genuine anginal pain, radiating to both arms, is sometimes combined with paroxysmal dyspnœa, as recognized by Osler (1897), Merklen (1908), and later by most writers on cardiac asthma (Pratt, 1926; Bedford, 1939).

Thirteen patients suffered from these combined paroxysms which were often but not always nocturnal. Pain occurred first and persisted until dyspnœa supervened, followed by some degree of pulmonary œdema. Nitrites were often given at the start of the attack and seemed to afford a measure of relief, but morphia was usually required. Like all forms of cardiac asthma, the anginal type complicates the terminal stages of heart disease, though the paroxysms may cease for a time with rest and treatment, or if congestive failure becomes established. The following example may be cited:

Case 100. Woman, aged 44, first seen in December 1938. No rheumatic or syphilitic history. Good health until 6 months earlier, when she became breathless on exertion.

Examination. Pulse, regular. B.P., 140/75. Arteries normal. Heart not appreciably enlarged; ascending aorta prominent (X-ray). Aortic diastolic murmur. EC., normal rhythm; T I negative. W.R. positive.

Course. Temporary improvement with rest in bed and oral anti-syphilitic medication. In February 1939, paroxysmal dyspnœa and admitted to hospital. There showed a series of severe anginal attacks, each succeeded by paroxysms of dyspnœa with blood-stained expectoration and transient signs of pulmonary œdema. Pain, sternal, spreading down both arms and of great intensity; morphine gave relief in 5 to 20 minutes. Frequent attacks of this kind for several weeks, the blood pressure falling progressively; died of left heart failure in March 1939.

Necropsy. Syphilitic aortitis, aortic incompetence, and almost complete occlusion of both coronary ostia. No macroscopic infarction of myocardium.

(*d*) *Syphilitic Status Anginosus.* The symptoms produced by stenosis or occlusion of the coronary ostia complicating aortitis, previously described as an " ingravescent anginal state " (Parkinson and Bedford, 1928), can usually be distinguished from the clinical syndrome of

coronary thrombosis or occlusion with massive focal cardiac infarction. Nine patients in this series presented the symptoms of ostial obstruction, and in 7 of them necropsies were obtained and confirmed the diagnosis.

Typically, a patient subject to effort pain begins to have spontaneous attacks which increase in frequency and severity, occurring in the daytime and at night. Repetitive seizures culminate in a status anginosus with falling blood pressure and often with dyspnœa and pulmonary œdema. It has frequently been stated that the duration of life from the first appearance of pain in these cases is a matter of months, but in only 2 of our fatal cases was it less than a year, the average being two years and the longest five years. Aortic incompetence is almost invariably present; in all our necropsies the cusps were deformed, though in one case clinical incompetence was absent, and in another it did not appear until shortly before death, and subsequent to the onset of repetitive anginal attacks.

One patient survived a status anginosus of the sort described. This was a woman, aged 34, with syphilitic aortic incompetence. Five months after the onset of angina of effort, she began to have spontaneous attacks of pain during the daytime and at night. While resting in hospital about 100 severe attacks were recorded and repeated doses of morphine were required. Gradually she became almost moribund, the blood pressure falling to 85/60 mm.; but after 6 weeks she began to improve slowly and later anti-syphilitic treatment was started. She left hospital and was still alive 6 years later, though subject to frequent anginal pain.

The following case is illustrative of the 8 who died.

Case 16. A man, aged 44, had complained for two years of a crushing pain in the chest on exertion, relieved by rest. Pain started at mid-sternum and spread to throat, down both arms, and to right scapula. Following an attack lasting half an hour, pain became more frequent and severe, occurring at night and apart from effort. Brought to hospital in a severe anginal seizure requiring morphia and lasting 7 hours.

Examination. Pulse, regular and collapsing. B.P., 140/50. Arteries, thickened. Aortic to-and-fro murmurs. No signs of congestive failure. W.R., positive. X-ray: gross enlargement of heart to left; aorta normal. EC.: inversion of T in leads I, II, and IV; later T inverted in all limb leads but upright in lead IV.

Course. Recurrent attacks of pain were followed by hæmoptysis and falling blood pressure. Some improvement, then status anginosus with sweating, dyspnœa, progressive collapse, and signs of pulmonary and systemic congestion. He died two years after he was first seen.

Necropsy. Heart: 25 oz.; general enlargement; ante-mortem clot in right auricular appendix. Syphilitic aortitis without much dilatation of aortic lumen; aortic cusps deformed and incompetent. Right coronary orifice completely occluded and left orifice severely stenosed. Coronary trunks patent throughout with only slight fatty atheroma. Some stenosis of orifices of innominate and left common carotid arteries. No naked-eye cardiac infarction. Infarcts of left lung.

The symptoms of syphilitic stenosis of the coronary ostia might be likened to those of coronary thrombosis in slow motion. The prodromal anginal attacks apart from effort extend over weeks or months, and the terminal state of collapse with failure develops gradually. When such a train of events is associated with syphilitic aortic incompetence, stenosis of the coronary ostia may safely be diagnosed. As already mentioned, cardiograms, though likely to be abnormal, rarely show the classical serial changes of cardiac infarction, and normal records may be obtained within a short time of death.

It is not suggested that ostial stenosis always causes anginal symptoms; there may be paroxysmal dyspnœa and failure without pain, or sudden unexpected death. Anginal pain occurred in 13 of Pincoffs and Love's (1934) 15 necropsy cases of ostial stenosis, in 23 of Cormia's (1935) 35 cases, and in 8 of Lamb and Turner's (1932) 19 cases.

(*e*) *Cardiac Infarction.* Ten patients in this series exhibited isolated severe anginal episodes corresponding to the classical syndrome of acute coronary occlusion, and accompanied by cardiographic signs of cardiac infarction. Only 3 had aortic incompetence. Though no post-mortem evidence is available in this group, it is probable that syphilis was no more than coincident with coronary atheroma and thrombosis. Published necropsy statistics show that such a coincidence is not rare (Lamb and Turner, 1932). Statistics of coronary thrombosis

give the incidence of syphilis as 5 to 10 per cent, but this probably includes cases of coronary ostial occlusion.

Anatomical Pathology of Syphilitic Angina

In the 12 cases that came to necropsy, 11 of the specimens were examined by one or both of us; the remaining necropsy was performed elsewhere and the state of the coronary ostia was not specifically recorded. The essential clinical and pathological data are given in Table II.

TABLE II

Clinical and Pathological Findings in 12 Cases of Syphilitic Angina Pectoris

Case	Age (at death) and Sex	Type of pain and clinical features	Post-mortem findings		
			Aortic incom.	Coronary ostia	Aorta
5	M/41	A.P. effort (5 months). Sudden death	+ relative	R. severe stenosis L. occluded	Aortitis, diffuse dilatation. Stenosis, L. carotid
12	F/43	A.P. effort (18 months)	+ not clinical	R. occluded L. severe stenosis	Aortitis, moderate dilatation
16	M/44	A.P. effort (2 years). Nocturnal and status anginosus	+	R. occluded L. severe stenosis	Aortitis, stenosis of innominate and L. carotid
21	M/45	A.P. effort (2 years). Nocturnal, paradyspnœic and status anginosus	+	R. } almost occluded L. }	Aortitis, diffuse dilatation. Stenosis innominate and L. subclavian
30	M/64	A.P. effort (3 years). Congestive failure. Sudden death	+	R. } patent L. }	Aortitis and atheroma; diffuse dilatation
34	M/60	A.P. effort (5 months). B.P. 260/130	+	Not recorded	Aortitis and dilatation
36	M/54	A.P. effort (3 years). Nocturnal and status anginosus	+	R. } severe stenosis L. }	Aortitis
45	M/48	A.P. effort (7 months)	+ slight	R. slight stenosis L. severe stenosis	Aortitis No dilatation
62	F/44	A.P. effort (8 years). Nocturnal (3 years). Sudden death	+	R. } severe stenosis L. }	Aortitis
75	M/56	A.P. effort (5 years). Paradyspnœic. Status anginosus	+ relative	R. severe stenosis L. slight stenosis	Aortitis Dilatation
95	M/38	Paradyspnœic A.P. (5 months). Congestive failure	+ gross	R. stenosed L. patent	Aortitis No dilatation
100	F/44	Paradyspnœic A.P. (1 month). Status anginosus	+	R. } almost occluded L. }	Aortitis Slight dilatation

Of the 12, 10 had angina of effort, 5 nocturnal angina, 4 paradyspnœic angina, and 7 a terminal status anginosus. All but one had clinical aortic incompetence. Necropsy showed syphilitic aortitis in every case, some degree of aortic dilatation without saccular aneurysm in 10, and deformity of the aortic cusps in all. Stenosis or occlusion of one or both coronary orifices was present in 10, absent in 1, and probably absent in the remaining case, though not specifically so recorded. Both orifices were involved in 9, and the right orifice alone in 1 case.

The right orifice was the more obstructed in 4, the left in 2, and they were equally involved in 3 cases. Thus, on the whole, the right orifice was slightly more involved than the left, as previous investigators have reported.

In many published post-mortem statistics relating to syphilitic aortitis, compiled by those who did not themselves examine the patient during life, painful symptoms are imprecisely or inadequately described. Analysis of such statistics has a limited value in relation to the pathogenesis of syphilitic anginal pain.

Gallavardin (1925) gives full clinical and pathological findings in 8 cases of syphilitic angina personally observed. On these, 7 had stenosis of or occlusion of one or both coronary ostia, 4 had aortic incompetence, and 3 had coronary atheroma. The single case with neither aortic incompetence nor ostial stenosis had atheromatous coronary obstruction, and the pathological evidence of syphilis was regarded as doubtful. Clinically these patients had often exhibited nocturnal and paradyspnœic anginal pain; a terminal status anginosus occurred in 2 of them. Lamb and Turner (1932) give necropsy findings in 18 cases of syphilitic angina. Eleven of them had aortic incompetence and all showed coronary pathology; 5 had ostial stenosis alone or combined with coronary atheroma, 9 had coronary atheroma (4 with thrombosis), and 1 occlusion of the right coronary orifice by aneurysmal pressure. Zimmermann-Meinzigen (1936), in 20 cases of syphilitic angina examined at necropsy, found coronary ostial stenosis in 15 and coronary atheroma with thrombosis in 2; most of them also had aortic incompetence.

Analysis of the post-mortem records of 58 cases of syphilitic aortitis from the records of the Bland-Sutton Institute of Pathology showed 14 cases of coronary ostial stenosis; 10 had angina pectoris, 2 died of failure without pain, and 2 suddenly, no clinical history being available. 12 of them had aortic incompetence. Anginal pain occurred in 16 of these 58 cases (28 per cent); 8 had aortic incompetence combined with stenosis of the coronary ostia, 3 aortic incompetence alone, 2 ostial stenosis alone, and 3 aortic incompetence combined with coronary atheroma or occlusion.

Massive localized cardiac infarction does not result from ostial occlusion, though sometimes patchy necrosis may be visible to the naked eye. All sections of the myocardium that we have examined have shown widespread microscopic areas of ischæmic necrosis or fibrosis of the myocardium. These myocardial changes resulting from ostial obstruction have been described in detail by Love and Warner (1934).

It has often been stated that anginal pain may occur in cases of uncomplicated aortitis, but the pathological evidence of this is no more convincing to-day than in Allbutt's time. We ourselves have not encountered any case of uncomplicated aortitis with intact coronary vessels at necropsy in which anginal pain occurred during life. Wilson (1937) from a study of uncomplicated aortitis concluded that it was a symptomless condition. Levy (1936) stated that cardiac pain is not to be regarded as a clinical manifestation of uncomplicated aortitis.

The essential pathological findings in syphilitic angina pectoris are, therefore, aortic incompetence or obstruction of the coronary ostia, or both together, combined with aortitis. Coronary atheroma may be associated with syphilitic aortitis, though it is rarely severe when there is ostial obstruction.

The Functional Pathology of Syphilitic Angina Pectoris

Allbutt's views on the aortic origin of anginal pain are too distorted by his uncompromizing opposition to the coronary theory to bear recapitulation to-day. But the hypothesis of an aortalgia simulating yet distinct from cardiac pain, a sort of syphilitic pseudo-angina, deserves serious consideration. Reid (1930) states that, in comparison with angina pectoris, the pain of syphilitic aortitis is not particularly under the sternum, is unrelated to effort, is of longer duration, and is apt to be nocturnal, but he admits that the distinction involves a

large degree of the personal equation. Others have described aortic pain as frequently accompanied by paroxysmal dyspnœa (Baric, 1912; and Longeope, 1913); as provoked by the dorsal decubitus (Laubry *et al.*, 1925); as unrelieved by rest (Stadler, 1932); and as unusual in distribution and occurring at rest (Coombs, 1930).

With regard to the distribution of pain, it was often widespread in our syphilitic cases, but not different from that of severe anginal pain in general. In other respects, however, the descriptions of aortalgia that have been cited may be accepted as applicable to our syphilitic patients. The pain was frequently nocturnal and unrelated to effort, tended to be prolonged, and when provoked by effort did not always subside quickly with rest. It was sometimes combined with paroxysmal dyspnœa. None of these features can be accepted as peculiar to syphilitic cases and it must not be overlooked that most of our patients were also subject to typical effort pain. Nocturnal attacks occur in about one fifth of all cases of angina of effort (Gallavardin, 1925); they were described as part of the disease by Heberden and have been accepted as such by subsequent writers. With regard to duration, spontaneous and nocturnal anginal attacks certainly last longer than the usual brief oppression due to effort. Prolonged pain occurs in coronary thrombosis and also in the course of progressive atheromatous coronary obstruction. Blumgart and others (1940) have used the term *coronary failure* to denote these severe and long anginal paroxysms which, occurring especially in cases of multiple coronary obstruction, they attribute to a prolonged but reversible cardiac ischæmia. Long duration is not, by itself, a valid reason for assuming that pain is aortic. Anginal attacks accompanied by paroxysmal dyspnœa or pulmonary œdema are certainly not confined to syphilitic heart disease. Those who regarded cardiac asthma as arising reflexly from the aorta, naturally explained associated pain in the same way. But present knowledge of the pathogenesis of cardiac asthma suggests a cardiac basis for paradyspnœic pain. As far as its clinical characteristics are concerned, therefore, there is nothing to exclude the paroxysmal pain of syphilitic aortitis being regarded as anginal and as explicable in terms of cardiac ischæmia.

Lewis (1929–31) has identified a special anginal syndrome in aortic incompetence and has cited examples of it previously described by Lauder Brunton and others. Its main features comprise tachycardia, transient elevation of blood pressure, relatively long duration, and prompt relief by nitrites. The attacks may be induced by effort, or may occur spontaneously after meals, at rest, or at night. One of Lewis's cases was syphilitic, but several of those cited were rheumatic. In our experience and in that of others (White and Mudd, 1927) spontaneous and nocturnal anginal attacks are common in cases of rheumatic aortic incompetence, where aortitis and coronary obstruction can often be excluded. It is usually held that the low diastolic pressure of aortic reflux predisposes to cardiac ischæmia by virtue of its adverse effect on coronary flow. Lewis postulated a general vaso-constriction involving the coronary vessels, and concluded that nitrites relieved the pain mainly by coronary vaso-dilatation. In many syphilitic cases, the pain undoubtedly corresponds to the type described by Lewis as peculiar to aortic incompetence.

Post-mortem statistics already cited indicate a high incidence of coronary ostial stenosis or occlusion in syphilitic angina (about 70 per cent), and an appreciable incidence of co-existent atheromatous coronary occlusion. Ostial stenosis is rarely found without aortic incompetence. In both conditions, cardiac ischæmia must be widespread throughout the heart, whereas in coronary atheroma it is commonly confined to the left ventricle, often to a small part of it. Such widespread ischæmia, once provoked, will not readily be relieved by a collateral circulation, as happens when it is limited to the territory of a single coronary branch. It appears that either stenosis of the coronary ostia or multiple atheromatous stenoses are capable of causing repeated and prolonged attacks of pain without any accompanying manifestations of acute cardiac infarction.

Nocturnal Angina Pectoris

So little is known of the mechanism underlying nocturnal angina that its special connection with syphilis deserves attention. Serial cardiograms are seldom practicable at night, but we have recently obtained records from a case of postural and nocturnal angina, though not, as it happens, of syphilitic ætiology. This was a man, aged 53, who for six months had suffered almost nightly from severe anginal pain, though scarcely troubled in the daytime if he avoided exertion. Sometimes pain would start in bed before he fell asleep, and might recur several times before morning. Abstention from all food in the evening reduced the attacks, and a normal evening meal aggravated them. Gradual relief was obtained by sitting upright or getting out of bed, and more rapid relief from nitrites, which he consumed freely. Clinical and radiological findings were normal; blood pressure always normal; W.R. negative; there was inversion of T III only. Anginal pain could often be provoked at will by lying flat for ten minutes, and serial records obtained in attacks so induced showed unquestionable evidence of cardiac ischæmia (Fig. 2). In this case ischæmic pain was undoubtedly excited by the horizontal posture, as happened in many of our syphilitic cases.

A thrust-up diaphragm or too good a supper was Allbutt's explanation of nocturnal

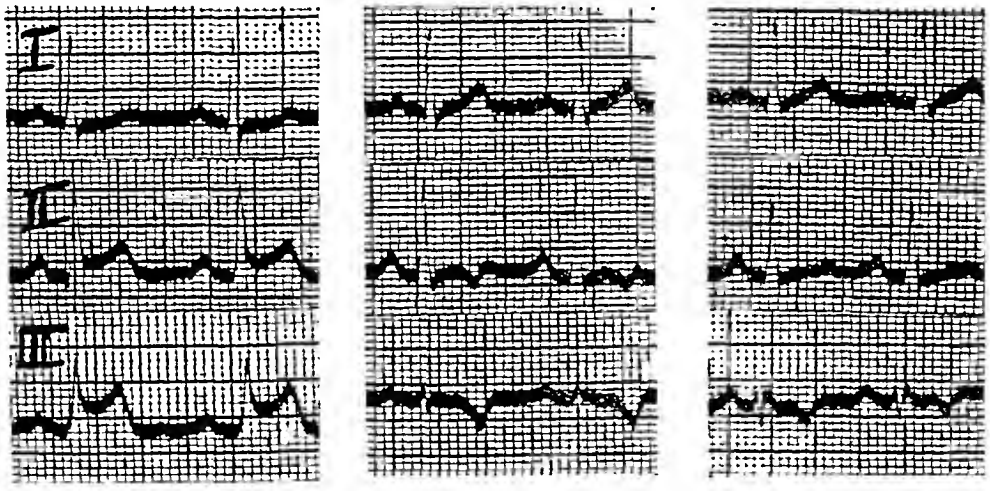

Fig. 2.—Serial electrocardiograms from a case of nocturnal angina in which attacks were provoked by lying flat. (A) During the pain; (B) Five minutes later; (C) Between attacks.

pain, and there is no doubt of the exciting influence of a full stomach. Wayne and Graybiel (1934) concluded that, in angina of effort, food acted by reflexly increasing the energy expenditure of the heart, and not by the mechanical effect of gastric distension. In a case of spontaneous angina, gastric inflation alone excited the attack. The recumbent posture, by elevating the diaphragm, may have a direct mechanical effect on the heart and aorta. In the so-called gastro-cardiac syndrome, pain of anginoid type is supposed to be due to bending of the aorta and tilting of the heart caused by a high diaphragm (Scherf, 1936). In the case of syphilitic aortitis, it is not difficult to believe that postural elevation of the diaphragm might cause or aggravate pressure pain from a grossly dilated aorta, as was suspected in several of our cases.

Assumption of the horizontal posture entails an increased cardiac output (McMichael, 1937) which, if maintained, would offer a simple mechanical explanation of nocturnal pain. But the relation of cardiac output to posture is complex and not yet finally settled. Hypercirculation at night was postulated by Eppinger and others (1924) in explaining cardiac asthma, and was attributed to peripheral vaso-dilatation.

A reflex nervous disturbance involving the heart is the alternative to a mechanical explanation of nocturnal pain in terms of posture. This might operate either by increasing cardiac energy

expenditure or by reducing coronary flow. It is evident that the spontaneous anginal attacks of aortic incompetence are associated with raised blood pressure, but the primary cause is difficult to decide. The fact that nitrites, by means of coronary vaso-dilatation, so readily abolish the pain, naturally suggests excessive coronary vaso-constrictor tone as a cause. Anrep (1936) believes that the relation between blood pressure and coronary vaso-motor tone is important in anginal states, and that a rise of pressure may produce a coronary vaso-constrictor response sufficient to overcome the direct effect of a higher filling pressure on coronary flow.

Paradyspnœic Anginal Pain. The French conception of angina of decubitus as a satellite symptom of paroxysmal dyspnœa, due to left ventricular distension, is usually credited to Merklen (Tessier, 1905), who certainly described this association (Merklen, 1908). He did not ignore the possibility of ischæmia as the cause of the pain, but suggested that a diffuse sclerosis of the whole coronary tree might cause both ischæmia and dystrophic damage sufficient to weaken the heart, which thus became *à la fois douloureux et faible.*

Congestive failure and cardiac pain are usually quite separate events. Congestion, pulmonary or systemic, is related to mechanical inefficiency of one or other ventricle; pain is related to an inadequate blood-supply of some part of a ventricle that is as a whole mechanically efficient. In paroxysmal dyspnœa the right ventricle must remain efficient; but if its blood supply is restricted, for example by ostial stenosis or low diastolic pressure, any increased resistance in the lungs might evoke ischæmic pain before or coincident with the onset of pulmonary œdema. The influence of posture is explained by the increased amount of blood in the lungs in recumbency. Once pulmonary œdema has occurred, anoxæmia must further predispose to pain. It is not difficult to understand that, in conditions of incipient left heart failure, postural circulatory adjustments may precipitate sometimes dyspnœa, sometimes pain, and occasionally both together.

The onset of paroxysmal dyspnœa at night raises much the same problems as does the onset of nocturnal pain. There is the mechanical explanation in terms of posture, and the reflex nervous theory. Wassermann (1926) regarded cardiac asthma as a reaction of the central nervous system to stimuli from the aorta, and stressed the associated autonomic nervous disturbances. The view that aortitis causes paroxysmal dyspnœa dates back to Huchard, yet there is no more pathological evidence that uncomplicated aortitis causes dyspnœa than that it causes pain (Keefer and Resnik, 1926). A predominance of vagal over sympathetic tone during sleep has been postulated (Eppinger *et al.*, 1924) and might favour coronary vaso-constriction, but this is purely hypothetical. If a reflex nervous origin of nocturnal angina is accepted as probable, at least in the case of aortic incompetence, the source of the exciting stimulus has yet to be determined.

Conclusion. The evidence reviewed suggests that generalized as opposed to focal cardiac ischæmia predisposes to spontaneous and nocturnal anginal pain, and that the horizontal posture is an important exciting cause. The *modus operandi* may be essentially mechanical or by way of reflex nervous reactions. In most cases of syphilitic aortitis, paroxysmal pain is ischæmic in nature and due to aortic incompetence often combined with stenosis of the coronary ostia. The response of pain to nitrites strongly supports this view. The possibility of pressure pain from a grossly dilated aorta being provoked by recumbency is admitted.

Course and Prognosis

War conditions have interfered with the follow-up of our cases, but many of them have been under observation long enough to permit some prognostic conclusions. Of 103 cases, 37 have died, 21 are untraced, 45 were alive when we began to analyse these records before the war, and a few of them have been seen since. The average duration of life from the onset of anginal pain in the 37 dead was 2·4 years; 7 survived more than 5 years, and one for 11

years. In the remaining 66 cases, 45 of which are alive and 21 untraced, the average duration of life from the onset of pain to the time they were last seen was 3·9 years. 27 of them have so far survived for more than 5 years and 5 for more than 10 years.

Though the expectation of life is appreciably less than in non-syphilitic angina, the outlook proved less gloomy than has been usually suggested. American statistics (Levy, 1936) give an average survival from the onset of symptoms in syphilitic aortitis of about 2 years or less, and German statistics are similar (Stadler, 1932).

With regard to the mode of death, 18 patients died in some form of anginal attack: 7 of them had a terminal status anginosus and 5 were reported as having " symptoms of coronary thrombosis "; 9 died in congestive failure, 6 died suddenly, and in the remaining 4, no details were available.

The effect of anti-syphilitic treatment was difficult to assess, but in general it did not remove the liability to anginal pain. If due allowance was made for the effect of rest and other routine measures, it was difficult to be sure that specific treatment appreciably influenced the anginal symptoms. In a few cases there was great improvement or even complete remission of symptoms for a time, and in a few others there was obvious aggravation of symptoms. On the assumption that it checks the progress of syphilitic inflammation in the aorta and thus prolongs life, we believe that anti-syphilitic treatment should always be given a trial, but aggravation of symptoms indicates its immediate cessation. Repetitive anginal attacks at rest or combined with paroxysmal dyspnœa are absolute contra-indications to anti-syphilitic treatment. The ordinary measures applicable to angina pectoris, such as rest in bed, sedatives, and nitrites, should not be neglected.

Summary and Conclusions

A series of 103 syphilitic patients subject to paroxysmal pain in the chest has been investigated with special regard to the clinical characteristics of the pain and its pathogenesis.

The age of onset of pain was evenly distributed over the fifth, sixth, and seventh decades, its maximal incidence being actually between 40 and 50 years. There were 80 men and 23 women, giving a sex ratio of 3·5 to 1. A history of syphilitic infection was obtained in 31 cases; the average period between infection and the onset of pain was 24 years. A positive Wassermann reaction was recorded at some stage in 96 cases.

The main clinical findings were aortic incompetence in 67 cases; dilatation of the aorta in 59; cardiac enlargement, often slight, in 83; and essential hypertension in 26. Abnormal cardiograms were recorded in 57 of 94 cases examined.

76 patients were subject to angina of effort and 64 had pain apart from effort. Nocturnal attacks were common and were usually independent of paroxysmal dyspnœa. They tended to be prolonged but were relieved by nitrites. Paradyspnœic anginal attacks occurred in 13, a syphilitic status anginosus in 9, and symptoms of coronary thrombosis, not attributed to syphilis, in 10 cases.

Post-mortem findings in 12 cases are given and other pathological data are considered. The essential lesions of syphilitic angina are aortitis and aortic incompetence, usually combined with stenosis or occlusion of the coronary ostia. Atheromatous and thrombotic coronary occlusion may be coincident with syphilitic aortitis. Pathological evidence that uncomplicated aortitis causes anginal pain is lacking.

The thesis of an atypical or pseudo-anginal syndrome due to aortitis is examined and rejected. Paroxysmal pain in syphilitic cases conforms to recognized clinical varieties of angina pectoris such as are encountered in non-syphilitic coronary and aortic disease. Aortic incompetence and obstruction of the coronary ostia, which affect the blood-supply to the whole heart, and cause widespread rather than focal cardiac ischæmia, predispose to spontaneous and prolonged pain. The horizontal posture appears to be an important exciting

cause of these nocturnal attacks. In paradyspnœic pain the effect of posture may be largely mechanical, but in other cases a reflex nervous mechanism may be operative. Consideration of certain cases also suggests that a relationship may exist between pressure pain from a dilated aorta and recumbency.

The clinical course, prognosis, and treatment are briefly described.

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BACTERIAL ANEURYSM

BY

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Stengel and Wolferth (1923) made an extensive review of the literature of mycotic or bacterial aneurysms. Since that time a number of cases have been recorded presenting unusual clinical or pathological features. Three new cases are described in the present paper, and, at the same time, nineteen cases reported since 1923 have been analysed.

PATHOLOGY

Most of the earlier theories as to the causation of bacterial aneurysms—a term that is preferable to mycotic which suggests a fungoid infection—laid emphasis on the mechanical production of this condition. Ponfick (1873) thought that the aneurysm was due to an embolus containing a spine of calcareous deposit which secured penetration of the vessel wall and allowed the entry of bacteria: no further evidence has been adduced to support this view. It was also suggested that, whilst embolism was the commonest cause, the aneurysm was produced by the mechanical effects of the embolus at the site of obstruction. Goodhart (1877) first advanced the hypothesis that infective processes were concerned. Since Eppinger's work (1887), it has been generally conceded that the aneurysm forms as a result of the bacterial infection of the vessel wall carried by the embolus, and is therefore more likely to occur in bacterial endocarditis and other septic conditions in which the emboli are heavily charged with bacteria. Emboli from infected valves tend to lodge, as Eppinger pointed out, at mechanical turns or sudden narrowings of the vessels. In smaller vessels it is reasonable to suppose, and has been demonstrated, that the embolus may be sufficiently large to block the vessel directly. Aneurysms in such cases are not very common because the blood ceases to pound against the damaged vascular wall. When a large vessel is affected, as in Case I of this paper, it is probable that the embolus lodges in the vasa vasorum, causing an area of infection and weakening at this point; the vessel is not obstructed and the arterial pressure rapidly produces an aneurysm in the weakened area. Usually it is not possible to identify the embolus or even the affected area post-mortem, owing to the rapid changes taking place in the vessel wall and the tendency to perforation with the formation of a false aneurysm, but there are well-established cases in which the embolus has been recognized. Eppinger found the same organisms present in the wall of the aneurysm and in the vegetations on the heart valves. In a more recent case, Lippincott (1940) identified cocci in the vasa vasorum in a case of aortic bacterial aneurysm. More rarely a bacterial aneurysm develops as a result of direct spread, along the intima of the vessel wall, of infection from neighbouring foci. A good example of this is seen in the development of aortic aneurysms arising from contiguous aortic valve lesions. Still less frequently aneurysms result from periarteritis, the arterial wall becoming infected from some external focus. Probably some such state of affairs prevails in the vessels in areas of tuberculous lung infiltration and is eventually responsible for the hæmorrhage.

In the present analysis of 22 cases, 13 showed positive signs of bacterial endocarditis.

The origin of the others was varied. Lippincott's case was associated with pneumonia, septicæmia, and septic arthritis. Aschner (1932) recorded one in which an aneurysm of the aorta resulted from an infective arteritis of uncertain origin; this was thought to be due to "metastatic ulcerous aortitis" and a gonococcus was isolated from a blood culture. In two cases the aneurysm was associated with a septicæmia of uncertain origin, and in another (Crane, 1937) sepsis of the foot appeared to be the focus of infection. In two cases trauma seems to have played a part. In one, recorded by Bain and Wray (1941), there was a suggestion of trauma resulting in rupture of the aortic valve, and this was followed by bacterial endocarditis causing an aneurysm from the base of the ruptured valve: the case might well be used as an example of aneurysm from spread of contiguous infection. In the second case (Taylor and Reinhardt, 1939) both sepsis and trauma were concerned; the aneurysm was in the right common iliac artery and developed as a result of pyonephrosis in association with the trauma of ureteric catheterisation.

Size.—The size of the aneurysm was often unrecorded, but when details were available the tumour rarely reached any considerable size unless by perforation it formed a false aneurysm. Such was the case in the writer's example of aneurysm of the femoral artery which attained proportions of 3–4 in. in length and 1·5 in. in diameter. Most bacterial aneurysms are not more than a few cubic centimetres in capacity. A remarkable exception was recorded by Mims Gage, an aneurysm of the common iliac artery reaching the size of a grape-fruit and being ligated during a period of bacteriological recovery.

Bacteriology.—Where a causal organism has been identified it was usually a streptococcus, as would be expected from the frequent association of bacterial aneurysms with infective endocarditis. Amongst rarer organisms, gonococci and typhoid and anthrax bacilli have been mentioned. In recording his gonococcal case, Aschner mentions that seven others had previously been described. A case of particular interest is that of Knighton (1937–8) in which the identified organism was *Bacillus abortus* causing a septicæmia with doubtful bacterial endocarditis.

Vessels Affected.—The site of bacterial aneurysm was stated by Stengel and Wolferth to be (in order of frequency) the aorta, abdominal arteries (superior mesenteric, splenic, and hepatic), and the cerebral and limb vessels. Mims Gage (1934) puts them in the following order: aorta, cerebral vessels, superior mesenteric arteries, and peripheral arteries, stating that the larger branches of the aorta are seldom involved. In the smaller series dealt with here, the aorta was again the most frequently affected. In 22 cases 8 involved the aorta, 3 the pulmonary artery, 2 the radial, 2 the common iliac, 2 the middle cerebral, 3 the mesenteric, 1 the popliteal, 1 the posterior tibial, 1 the femoral, 1 the axillary, and 1 the mitral valve. Often aneurysms occurred in more than one vessel, though this does not appear to be so frequent as is suggested by Eppinger. Prior to 1923, the number of cases of bacterial aneurysm of the pulmonary artery was comparatively small (in Stengel and Wolferth's series 14 out of 217 cases) and it is of interest to note that in this small series there is a relatively high incidence.

Associated Lesions.—The majority of aneurysms previously recorded seem to have been associated with common valvular lesions due to bacterial endocarditis. Amongst the 22 cases analysed here there was rather a high incidence of congenital defects, namely, 5 cases, including 1 of cor triloculare, 2 of coaretation of the aorta, and 1 of hypoplasia of the aorta. Two cases (one with coarctation) were suffering from patent ductus arteriosus. Probably these cases give a false impression of the frequency of congenital lesions as they were no doubt published partly on account of their rarity.

Clinical Manifestations

Age and Sex.—In the present series the average age was only a trifle higher than previously recorded, namely 33. Mims Gage (1934) states that most cases occur before the age of 30,

whilst Stengel and Wolferth showed the second, third, and fourth decades to be the commonest, as contrasted with the fifth decade, the commonest for syphilitic aneurysms. Males preponderated over females, as in the series analysed by Stengel and Wolferth.

Incidence.—Bacterial aneurysms are uncommon, though if detailed autopsies were possible in all cases of bacterial endocarditis, no doubt more would be found. Garland (1932) in 12,000 autopsies found 2·2 per cent of aneurysms, of which only 4 were bacterial in origin. In the examination of some recent records of bacterial endocarditis from the files of the Royal Infirmary and Smithdown Road Hospital, Liverpool, no case of bacterial aneurysm was found except those reported here.

Course.—Some attempt has been made to determine how long the aneurysms take to develop and the duration of life thereafter. This was not easy owing to the insidious and variable course of bacterial endocarditis. In most cases it would appear that the septicæmia was present for a few months before the aneurysm was detected, but that the aneurysm itself only took a few weeks (up to two months) to attain a recognizable size. Sometimes it was possible to date the beginnings of the aneurysm by a clear history of embolism. Once present, the course of the aneurysm was usually very rapid and death generally took place within six months. Not only do bacterial aneurysms seem to occur in the more severe cases of bacterial endocarditis, but in themselves constitute a complication of great gravity owing to the risk of rupture with hæmorrhage and of vascular obstruction in the case of limb vessels. Occasionally recovery takes place. In this series three cases are recorded in which the patient was still living at the time of publication. The case of Mims Gage has already been mentioned. Nicholson (1940) described a case of coarctation of the aorta in a child of 12 with arrested subacute bacterial endocarditis and a calcified bacterial aneurysm at the seat of stricture; treatment had only been symptomatic. In another case (Knighton 1937–38) there was a clear history of embolic obstruction in the right axillary artery occurring during the course of an abortus infection in which there was also aortic regurgitation and mitral disease; after the septicæmic symptoms subsided the aneurysm continued to enlarge but was dealt with by ligation. The heart lesions, of course, persisted, leaving the prognosis uncertain.

Diagnosis.—The diagnosis of bacterial aneurysms is often impossible especially in the case of deep-seated arteries. Aneurysms of the superficial arteries, open as they are to inspection and palpation, are more easily recognized and many more might be observed if careful observation of these vessels were made during the course of bacterial endocarditis. In the present series, 6 out of 7 peripheral aneurysms were recognized clinically. In the seventh an aneurysm of the radial artery was incised as an abscess (Areta, 1935). Of the aortic aneurysms only one was recognized, that recorded by Nicholson (1940) and already described; the diagnosis depended upon radiological identification of the calcified sac. In one of the original cases described by Stengel and Wolferth, the clinical diagnosis of a bacterial aneurysm of the aorta was made by the great pulsation in the upper chest and an increase in vascular dullness in a case of bacterial endocarditis. The possibility of embolic aneurysm of the cerebral vessels has sometimes been considered when localizing signs have pointed to a sudden vascular lesion of the brain during the course of bacterial endocarditis but confirmation is impossible. Such aneurysms frequently rupture so that to the embolic features there may be added symptoms due to cerebral hæmorrhage. This is illustrated by the case of Koch and Nuzun (1940) in which an aneurysm of the right middle cerebral artery resulted from embolism during a subacute bacterial endocarditis. Subarachnoid hæmorrhage or cerebral abscess was suspected from the physical signs and the presence of blood in the cerebro-spinal fluid supported the former diagnosis.

Embolism into the mesenteric vessels is notoriously difficult of diagnosis, usually suggesting some acute abdominal catastrophe, but the possibility should not be overlooked in view of the practical importance in saving the patient an unnecessary operation. In one of

the new cases recorded here the diagnosis was suspected whilst the patient was in hospital with bacterial endocarditis.

Treatment.—The treatment of bacterial endocarditis is most unsatisfactory even since the introduction of sulphonamide and allied therapy. It follows that bacterial aneurysms, commonly associated with bacterial endocarditis, are even less susceptible to treatment. In spite of this, out of 22 cases reviewed here, ligation of the aneurysms was possible in 2, in which the bacterial endocarditis was healed or apparently quiescent. It may be, therefore, that the development of sulphonamide therapy will lead to more cures of bacterial endocarditis and thus arrest the formation of aneurysms or permit of their surgical treatment if they develop. A great difficulty will always be the rapid development of the aneurysm to the point of rupture.

Notes of Three Cases

Case 1.—Femoral Aneurysm.

Admitted 1/9/1941 with history of pulsating swelling in left groin noticed the day before, preceded by soreness for one week. Rheumatic fever when aged 13 with occasional tonsillitis. Father said to have died from bursting of an aneurysm, ? aortic.

Condition on admission. Aged 35. General condition poor. Remittent pyrexia. Numerous petechiæ. No splenic enlargement. Heart: well marked aortic regurgitation. Urine: some red blood corpuscles and leucocytes. Sedimentation rate: rapid fall. Blood count: R.B.C., 3,200,000;

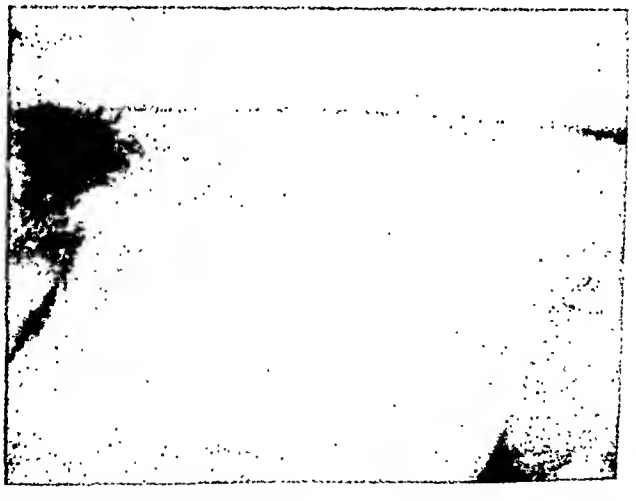

Fig. 1.—Case 1. Photograph, taken during life, showing the femoral aneurysm.

W.B.C., 9,000; Hb., 50 per cent. Gonococcal complement fixation test, positive. W.R., negative. Blood cultures, sterile. A diagnosis of bacterial endocarditis with bacterial aneurysm of the femoral artery was made.

On 19/9/1941, patient mentally confused, emaciated, and pale. Extensive purpura mainly of the trunk but including eyelid conjunctiva. Rough aortic systolic murmur with thrill, in addition to diastolic murmur of regurgitation previously found. Aneurysm larger. Loud rasping systolic murmur with thrill over the sac. Systolic and diastolic murmurs just above sac in the groin.

The patient died on 27/9/1941.

Post-mortem report. (Dr. C. V. Harrison.)

An emaciated man, rather pale, with innumerable petechial hæmorrhages about 3 mm. diam. scattered over body, especially over trunk. In the upper part of Scarpa's triangle on the left there is an ovoid swelling about 5 × 7 cm. (Fig. 1). Rigor mortis incomplete.

Cardiovascular System. Pericardium contained an excess of clear fluid. Heart slightly hypertrophied, 13½ oz. (364 g.). Tricuspid and pulmonary valves normal. Mitral valve, old rheumatic fibrosis and slightly stenosed (admits one finger). Infective endocarditis in the form of relatively flat warty vegetations, which have begun to spread on to the posterior auricular wall. Aortic valve also old rheumatic fibrosis and infective endocarditis similar to mitral; vegetations have spread

FIG. 2.—Case 1. The heart, showing vegetations on the aortic and mitral valves, due to acute bacterial endocarditis.

down on to the upper part of the interventricular septum and also on to the aortic aspect of the aortic cusp of the mitral valve. Myocardium of left ventricle, minute points of fibrosis up to 1 mm. diameter. Coronary arteries normal. Aorta, early atheroma.

Respiratory System. Each pleura contains about 200 c.c. of clear fluid. Both lungs show œdema and there is a little early broncho-pneumonia in the upper part of the lower lobe of the left lung.

Spleen. About normal size. About two-thirds of it substance infarcted, the infarcts being large and starting to break down in the centres (Fig. 3).

Kidneys. Both show a number of infarcts. Some small and fibrosing, others larger (up to 1·5 cm.) and recent. The right shows splotchy congestion, the left does not.

Ureters, bladder, etc., normal.

Alimentary tract and pancreas, normal. Liver, some acute congestion.

In the *left groin* there is an aneurysm of the left femoral artery arising just below Poupart's ligament. This is about 5×5×7 cm. The anterior crural nerve is splayed out over it (Fig. 4). Apparently the aneurysm has either burst or leaked posteriorly because blood is ploughing up the muscles.

The specimen was dissected out en bloc and left to fix before opening.

Summary of Lesions. (1) Infective endocarditis superimposed on old rheumatic fibrosis of aortic and mitral valves. (2) Mycotic aneurysm of left femoral artery. (3) Infarcts of spleen and kidneys. Further dissection of the aneurysm after fixation showed that it had burst and that the wall of the

FIG. 3.—Case 1. Spleen showing numerous infarcts.

FIG. 4.—Photograph of aneurysm after dissection. Shows anterior crural nerve splayed over the mass which is chiefly due to a "false" aneurysm from leaking of original sac.

sac was now formed by the adjacent muscles. No remnants of the artery wall being visible in the parts examined.

Case 2. *Radial Aneurysm.* . (Dr. Norman Capon's case.)

Man, aged 42. Symptoms for about three months. Anorexia, sweating, pain in the joints, fever for probably about two months.

On 7/9/1934 very severe pain in left forearm, with nothing to show for it.

On 13/9/1934 admitted to hospital. Mitral presystolic murmur. Petechial hæmorrhages. Negative blood culture. No splenic enlargement.

On 19/10/1934. Small aneurysm on front of left forearm. Blood culture repeated—negative. Patient left hospital at own request.

On 29/1/1935 the patient died at home. Dr. Rowlands reports that he became progressively weaker and finally had convulsions, ? due to intracranial embolus.

Case 3. *Mesenteric Aneurysm.*

Present History. A male, aged 23, working long hours as a clerk, was admitted on 11/12/1942. Rheumatic fever, when 7 (many weeks in bed), when 14, and again when 15. One attack since.

Tired and run down for past two months. Fleeting rheumatic pains a month ago. Red painful patches on the finger pads lasting a few days. Dr. Edwards noted fever a month ago and has kept him in bed since. Drenching night sweats, increasing pallor.

Severe abdominal pains since this morning. Vomiting, no blood. No diarrhœa or melæna.

On examination. Marked pallor. No finger clubbing, no petechiæ. Pulse rate, 110. Apex beat two inches outside nipple line; forcible. Blowing aortic diastolic murmur. Diffuse abdominal tenderness and rigidity.

Urine. A small amount of albumen; a moderate number of squamous cells, fair number of red cells, an occasional leucocyte, and a small number of cocci.

Clinical Diagnosis. Subacute bacterial endocarditis; mesenteric embolism.

On 14/12/1942 at 10 p.m. he was comfortable and had improved since admission. At 11.15 p.m. he collapsed. When seen, comatose with stertorous breathing and profuse sweating. His blood count showed 35 per cent hæmoglobin with a well-marked polymorphonuclear leucocytosis (polymorphs, 82 per cent; total leucocytes, 43,600).

He died at 1.20 a.m. the following morning.

Post-mortem report. (Dr. C. V. Harrison.)

Subacute infective endocarditis. Old rheumatic endocarditis. Mycotic aneurysm of mesenteric artery. Hæmoperitoneum. Very pale. Rigor mortis present. Abdomen rather full. No other lesion.

Abdominal cavity: Distended with enormous quantities of fresh blood.

Heart: Right side normal. Mitral valve thickening but no shortening. No stenosis or apparent incompetence. Slight thickening of posterior auricular wall. Left ventricle hypertrophied and dilated. Aortic valve old rheumatism and infective endocarditis, the latter on the aortic aspect of the aortic cusp of the mitral and the adjacent cusp of the aortic. It took the form of an ovoid, almost " puff ball " thrombus attached to the aortic valve with granular vegetations adjacent to it.

Blood vessels: There was an embolus in one of the main branches of the mesenteric artery. This had caused a mycotic aneurysm in the mesentery corresponding to the last two feet of small intestine. This had burst on its posterior aspect with a massive hæmorrhage.

Small intestines: Normal in spite of the aneurysm of the mesenteric artery. Stomach, colon, and appendix : normal.

Spleen : Shows a reaction in the form of a pale cellular pulp with not much softening.

Kidneys: Right kidney showed one healing infarct and a few minute petechiæ. Left kidney showed a few petechiæ. Ureters, bladder, and prostate, normal.

Summary

Three new cases of bacterial aneurysm are described, one of the femoral artery, one probably of the radial artery, and one of the mesenteric artery. The last ruptured, causing death from hæmorrhage into the peritoneal sac. The post-mortem findings are recorded in two cases.

Another nineteen cases have been collected, cases reported since 1923 when the subject was fully dealt with by Stengel and Wolferth. These have been analysed.

I am indebted to Dr. J. P. Steel for access to Case 1 and to the case sheets of Smithdown Road Hospital in search for further aneurysms. Professor Henry Cohen also allowed me to scrutinize his notes of recent cases of bacterial endocarditis. Dr. Capon kindly supplied the notes for Case 2 and Dr. G. Sanderson those for Case 3. Dr. C. V. Harrison performed the post-mortem examinations on Cases 1 and 3.

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HEART CHANGES IN ALKALOSIS

BY

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Electrocardiographic findings in alkalosis were first noted in 1922 by Carter and Andrus, who observed that the Q–T interval was prolonged by more than 30 per cent in three of their cases; this was associated with a lowering of the blood calcium. Barker, Arbor, Shrader, and Ronzoni (1939) produced artificial alkalosis by voluntary overventilation or by ingestion of sodium bicarbonate, the Q–T interval being slightly increased by the latter procedure. In a hysterical patient with hyperventilation a similar effect was produced, but this did not exceed normal limits; a reduction of the T wave was also observed.

An opportunity occurred recently of studying the cardiac function in alkalosis.

CASE REPORT

A woman of 47 was admitted to St. Nicholas Hospital on December 4, 1941. She stated that she had been well till three years previously when she began to suffer from occasional vomiting after meals and during the night. Abdominal pain was troublesome at times and was relieved by vomiting or alkalis. Since then she had never been free from the trouble for more than a day at a time. For the few weeks before admission the severity of the attacks increased and she took MacLean's powder frequently. On the day before admission she suddenly felt as though about to die and her hands and arms went into spasms and felt numb and tingling. This soon passed off, but returned the following morning. On admission, both arms were found to be in tonic spasm with elbows and wrists flexed, fingers and thumb in the position of *main d'accoucheur*. The abdomen was held tense. Blood taken at this time had a bicarbonate content of 150 vol., a blood urea of 132 mg., and a serum calcium of 10·2 mg., each per 100 c.c. Next day she became confused, disorientated in time, suspicious, and apprehensive. At this time she was having repeated cramps in her limbs and her tongue was dry and thickly coated. After administration of 5 c.c. of 5 per cent calcium chloride intravenously, she improved considerably.

On the third day in hospital she was again restless and confused, and kept trying to get out of bed with the intention of going home. Every piece of paper she could lay hands on (including her case notes) she would fold up and put in her bag. During the course of the morning she vomited three pints of greenish fluid. On examination she was found to be very emaciated, but had a good colour. The Chvostek sign was negative, Trouseau faintly positive. The blood pressure was 100/60. The heart was regular at a rate of 75; the two sounds were unusually close together but the apex beat was not displaced. The abdomen showed marked peristalsis, apparently gastric in origin, over almost its entire extent, and splashing could be elicited over a wide area. The temperature was 98·8°, respirations 22. The urine was neutral and contained much albumin. A cardiogram showed low voltage complexes in lead I and a greatly prolonged Q–T interval (0·56 sec.).

The serum bicarbonate at this time was 150 vol., chloride 166 mg., sodium 320 mg., and blood urea 310 mg., each per 100 c.c.; the B.S.R. was 52 mm. in the first hour and the circulation time (arm to tongue) 30 seconds.

An intravenous drip of 2 per cent saline at 120 drops a minute and stomach wash outs with saline were started. Improvement was rapid and by the fifth day the patient was normal mentally and less dehydrated in appearance. The serum bicarbonate had now fallen to 135 vol. and the chloride risen to 282 mg. and the blood urea was 210 mg., each per 100 c.c. A barium meal showed a large stomach with increased peristalsis, with obstruction at the pylorus, and a small prepyloric ulcer. By the seventh day the serum bicarbonate was 125 vol., chloride 319 mg., sodium 305 mg., and urea 42 mg., each per 100 c.c. On the eighth day, laparotomy was performed by Mr. Martin under local anæsthesia and pentothal. There was much prepyloric scarring with no ascertainable patency from

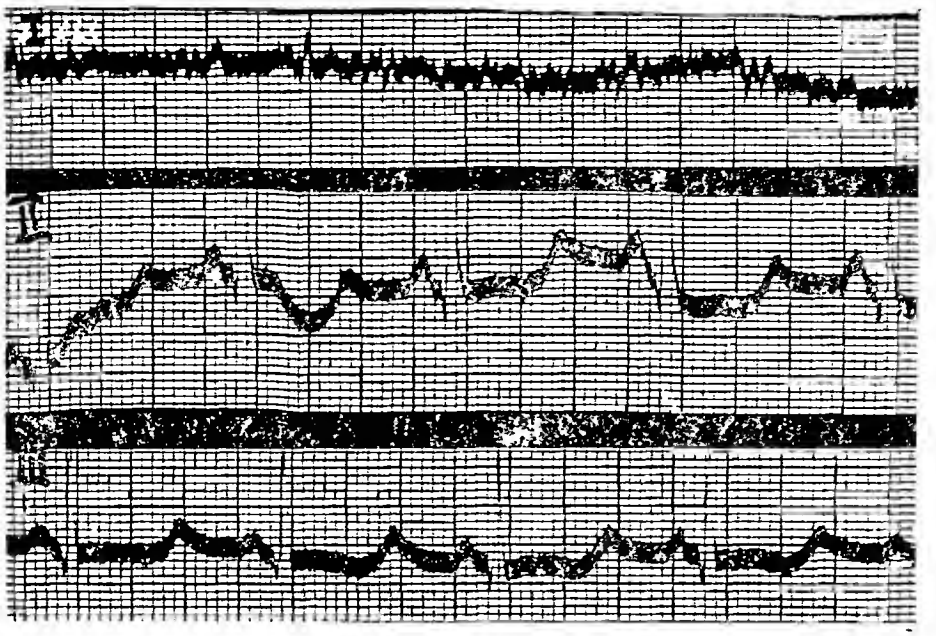


FIG. 1.—Electrocardiogram showing prolongation of the Q–T interval (0·56 sec.). There are some extrinsic excursions, especially in lead II.

external tests. The stomach was enormously dilated. A gastro-enterostomy was performed. During the operation the pulse became very feeble, the veins in the neck engorged, and the breathing shallow and infrequent; cyanosis was present despite a very light stage of anæsthesia, but oxygen resulted in a rapid improvement which was maintained for the remainder of the operation. Despite continued administration of saline intravenously the patient died two days later. A post-mortem examination was refused.

DISCUSSION

Bazeft (1920) was the first to use the electrocardiograph to study the duration of systole in relation to the heart rate. He measured the Q–T interval (from beginning of Q to end of T) in lead II in a number of normal men and women, expressing the result by the formula: duration of systole $=K\sqrt{\text{duration}}$ of cardiac cycle. K was found to average 0·37 in men and 0·40 in women, the limits being 0·36 to 0·48. An increase of the relative length of systole has been found in conditions associated with hypocalcæmia, notably hypoparathyroidism, and to a less extent in diabetic coma, rheumatic carditis, cardiac enlargement, heart block, and chronic nephritis, according to Graybiel and White (1941). Hypocalcæmia would also explain the changes noted in their cases of alkalosis by Carter and Andrus. In the present case the Q–T interval was 0·56 sec. and the cycle 0·8 sec., so that K=0·63, a very considerable increase; so great in fact that systole is twice as long as diastole instead of shorter than it. This resulted in a reversal of the heart sounds, the second occurring just before the first. As a consequence of the short diastole and inadequate filling of the ventricles, the first sound was short and sharp like a normal second sound, and therefore readily mistaken for it. The apparent proximity of the two sounds is explained by the fact that diastole is actually shorter than normal systole, as shown by calculating K, using diastole instead of systole in Bazett's formula, when K is found to be 0·27 (normal systole 0·36–0·44). The blood calcium was normal in this case, but there may have been a diminution of diffusible calcium (as has been postulated to explain the occurrence of tetany in alkalosis). Dehydration was here a pronounced feature, as it is also in diabetic coma and at one stage of chronic nephritis, and these two conditions are sometimes associated with prolongation of systole. Bazett's formula was

S–T segment. In several cases this became elevated, sometimes being bowed with the convexity downwards (Fig. 1 A). These elevated curves simulate those of coronary thrombosis. Later the segment becomes a steep rising one to the increased T wave. (See Fig. 1 B).

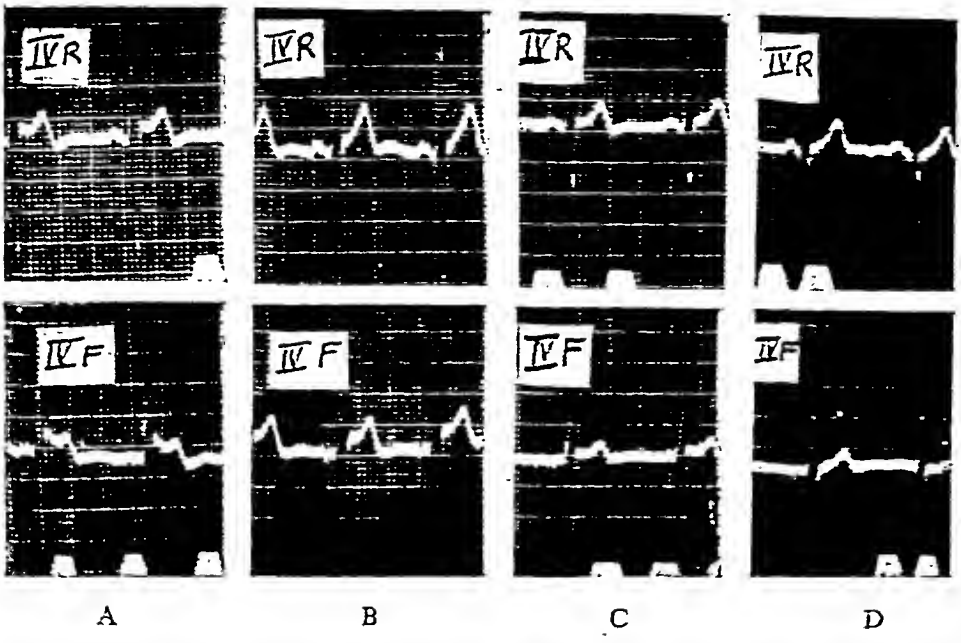


FIG. 1.

(A) Effect of plasmoquin on the electrocardiogram. The patient was taking 1/6 grain, b.i.d.
(B) Effect of plasmoquin, 1/6 grain, b.i.d., for 7 days.
(C) Effect of atebrin, 1·5 grains, b.i.d., for 7 days.
(D) Effect of quinine, 7 grains, b.i.d., for 5 days. All these figures are from the same patient.

Atebrin

P wave. This was generally decreased, sometimes to half the previous size in lead IV R.

P–R interval. This was unaffected.

QRS wave. The Q wave may be increased in amplitude; the R and S waves were generally decreased in amplitude.

T wave. This was markedly depressed in all cases, and sometimes in leads IV R and IV F, by as much as 70 per cent of normal (Fig. 1 C).

S–T segment. Atebrin restored this to iso-electric level after elevation by plasmoquin.

Quinine

P wave. This was decreased, but not to the extent seen in the atebrin effect.

P–R interval. No effect.

QRS and S–T. There was no constant effect on Q or on the S–T segment, but R and S were decreased in amplitude in both IV R and IV F (Fig. 1 D).

T wave. This was markedly decreased, though less than by atebrin. Often a small negative phase followed the initial positive phase.

SUMMARY

The effects of plasmoquin, atebrin, and quinine on the electrocardiogram of convalescent malarial patients has been investigated.

Plasmoquin increases the amplitude of the various deflections, affecting the T wave most

markedly and constantly. In some cases the most striking feature is the effect on the S–T segment which simulates the cardiogram of coronary thrombosis. Whether this is due to an effect on the coronary circulation, we are not in a position to state.

Atebrin decreases the amplitude of the various deflections, also affecting the T wave most markedly and constantly. It restores the S–T segment to the iso-electric level after it has been elevated by plasmoquin.

Quinine has an effect similar to atebrin but to a lesser degree.

Differentiation between the effects of plasmoquin on the one hand, and of atebrin and quinine on the other, in a particular patient may be made on the cardiographic findings given above. Plasmoquin increases the size of the T wave above normal while quinine and atebrin decreased it below normal. Plasmoquin often has an effect on the S–T segment, as described ; this is not seen in the exhibition of either of the other two drugs.

A CASE OF SUBENDOCARDIAL INFARCTION

BY

R. KEMBALL PRICE AND L. R. JANES

Received May 3, 1943

Disease of the coronary arteries, by commoner occurrence or by more frequent diagnosis, is assuming increasing importance in clinical medicine. The following case is reported because it shows some interesting features, and full clinical, cardiographic, and pathological investigation was possible.

A schoolmaster, aged 55, was admitted to hospital on November 16, 1941, with a three weeks' history of increasing angina of effort. Clinical examination showed nothing abnormal except a blood pressure, 155/100; W.R. negative. After admission to hospital he continued to have short attacks of pain relieved by amyl nitrite, after some of which T wave inversion in leads I and IV persisted for several days (Fig. 1). He was nervous and irritable, and attacks were usually precipitated by annoyance over some imagined grievance against other patients in the ward. Cardiograms taken during an attack on December 11 showed inversion of T IV, and 10 minutes after amyl nitrite, recovery of T IV to the upright position (Fig. 2). On December 20, the patient had a prolonged attack of pain not relieved by amyl nitrite, after which attack the cardiogram showed persistent T wave inversion in leads I and IV (Fig. 3).

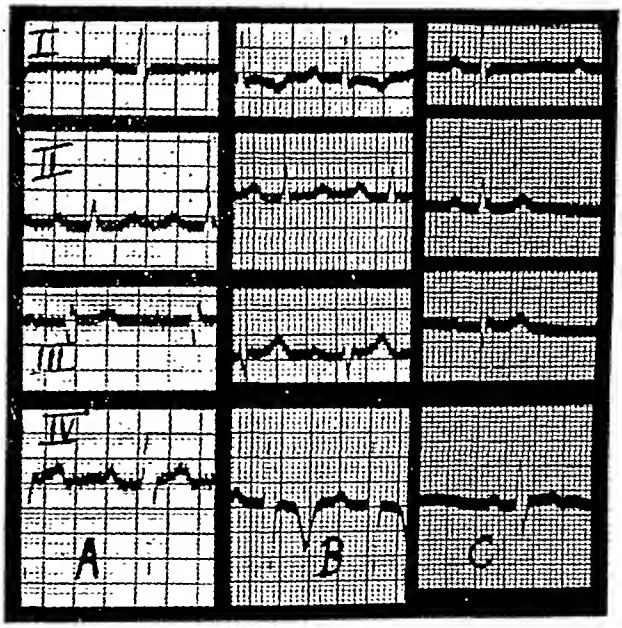


FIG. 1.—(A) Before attack (12/11/41). (B) Three days after attack of pain lasting 2 hours (17/11/41). (C) Return towards normal, 12 days later (29/11/41).

He made satisfactory progress and the blood pressure stabilized at about 150 mm. He started to get up on February 6, six weeks after his infarct.

Two days later, February 8, a severe attack of pain across the chest commenced at 6 a.m., and after failure to obtain relief from amyl nitrite, 1/4 grain of morphia was given and the dose repeated two hours later. At 11 a.m. he was seen by one of us (R. K. P.) and as he was still in great pain another quarter of a grain of morphia was given intravenously. This gave rapid relief and he was alseep within ten minutes. He woke again one and a half hours later and complained of pain and a further 1/4 grain of morphia was given subcutaneously. After this he remained comfortable.

An electrocardiogram taken the following day showed RS–T distortion with elevation

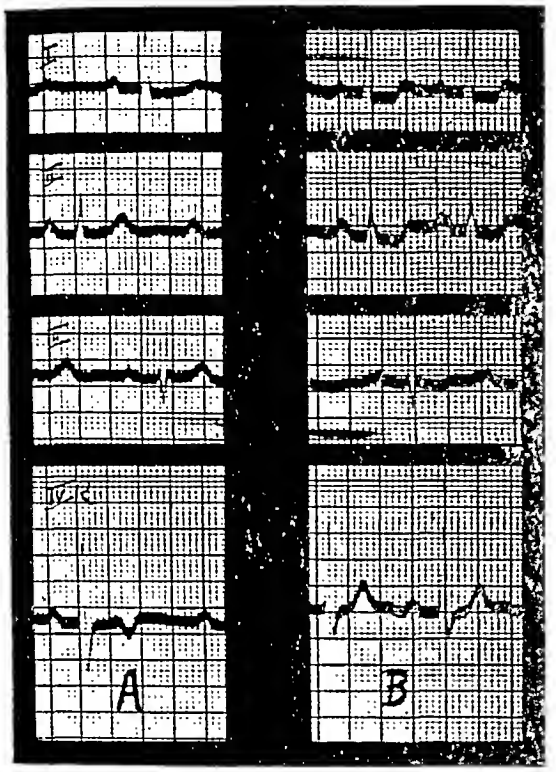


FIG. 2.—(A) During an attack of pain. (B) Ten minutes later, after amyl nitrite (11/12/41).

in leads II and III, with inversion of T waves. His blood pressure remained low 90–100/70–80, and on February 14, six days later, he began to complain of shortness of breath. The quality of the heart sounds deteriorated and on February 16, gallop rhythm was heard at the apex and rales were detected at the bases of the lungs. The pulmonary œdema cleared temporarily after injections of neptal, but the patient's general condition became worse. On February 26, a blowing systolic murmur became audible at the apex and persisted. He developed acute pulmonary œdema on March 3, and died within a few minutes, three weeks after the second infarction.

SYNOPSIS OF AUTOPSY

The deceased was a heavily-built obese man. No œdema of the feet nor ascites was present. There was acute œdema of the lungs with 140 c.c. of non-fibrinous straw-coloured fluid in each pleural cavity. The liver showed early chronic venous congestion. The kidneys appeared normal. The pancreas was very fatty. A hydrocele of the left testis was present.

The heart was enlarged and weighed 567 g., due to left ventricular hypertrophy. Considerable pericardial fat covered the heart. There was no pericarditis or endocardial exudate. The aortic valve was competent but atheroma was present at the base of the mitral and aortic cusps. Considerable atheroma of the aortic arch and of much of abdominal aorta was found. Atheromatous fatty streaking of the pulmonary arteries and their main branches was present.

The main coronary arteries showed much atheroma but no actual occlusion. There was extreme atheromatous narrowing, one inch from the opening into the aorta, of the right coronary artery, and similar narrowing of the left coronary artery one-third of an inch from its origin.

Focal disseminated fibrosis was present in the left ventricular muscle in its left outer border throughout its length, and also in the anterior wall near the junction with the inter-ventricular septum in the proximal part of the left ventricle near the base of the heart.

There was a large "sheet-like" subendocardial infarct extending from the base of the left ventricle at the auriculo-ventricular ring to the apex, involving the posterior wall of the left ventricle including the posterior papillary muscle, and the interventricular septum throughout its length, and extending on to the anterior wall of the left

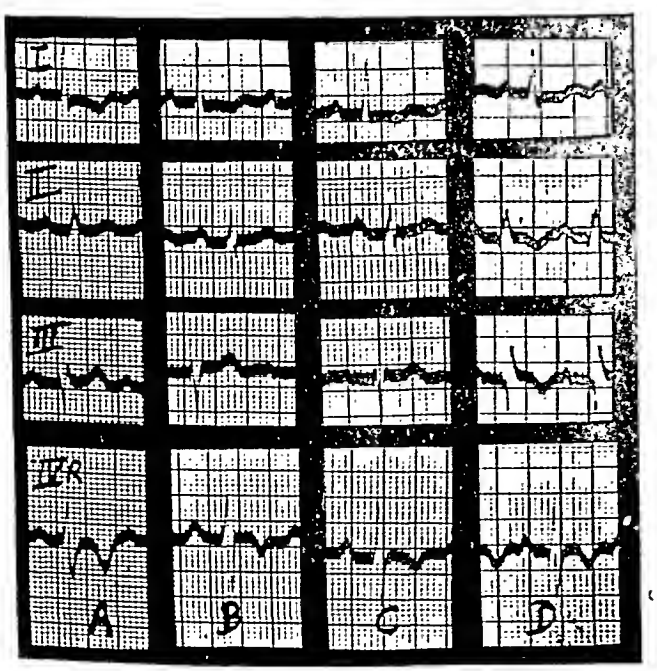


FIG. 3.—(A) Two days after prolonged attack of pain (22/12/41). (B) Before amyl nitrite (5/2/42). (C) After amyl nitrite (5/2/42). (D) One day after attack of pain lasting 5 hours (9/2/42).

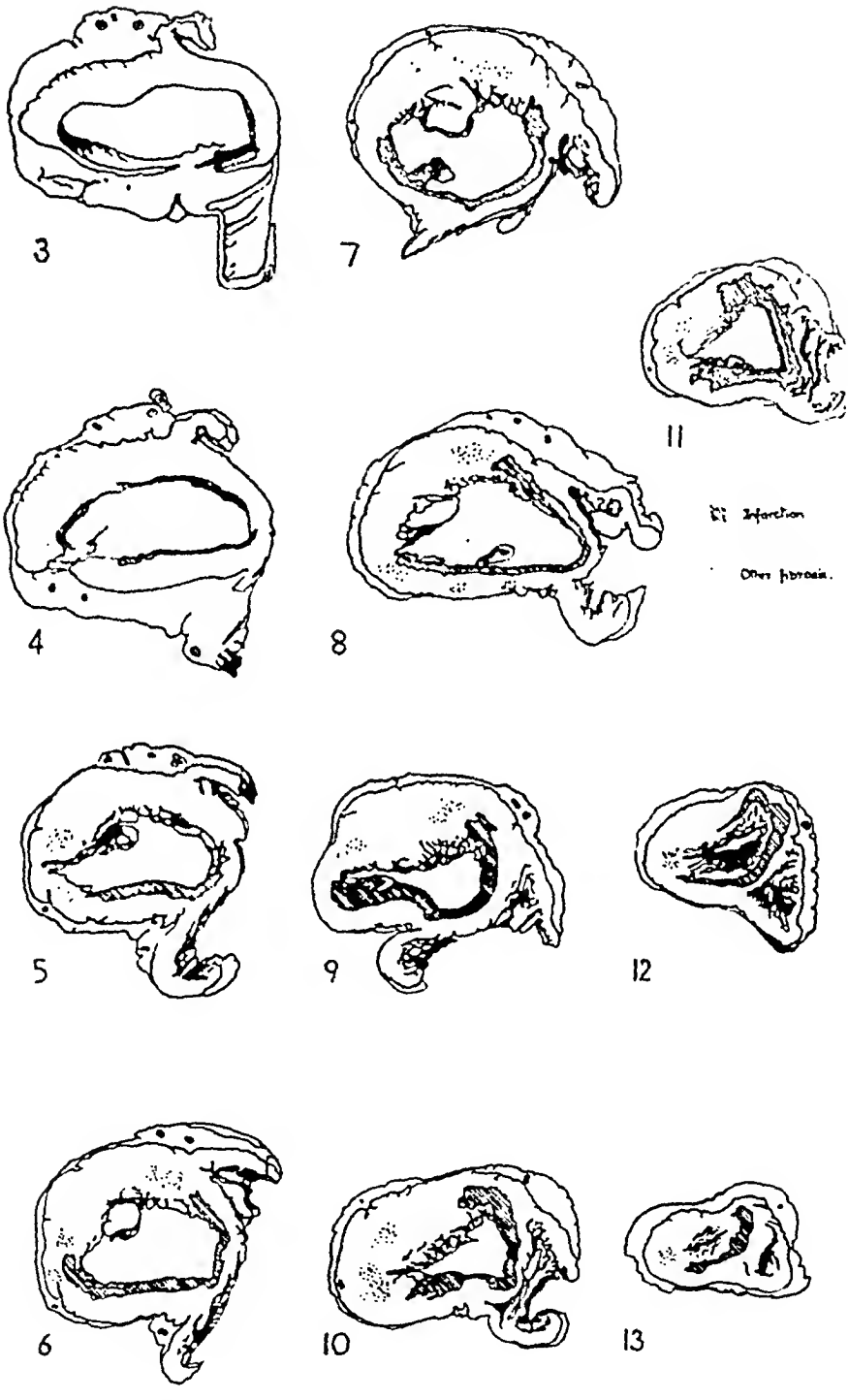


FIG. 4.—Photograph of a series of drawings of transverse sections through the ventricles, made at intervals of approximately 5 mm., extending from the atrio-ventricular ring (No. 3) to the apex (No. 13). The sheet-like recent infarct is shown cross-shaded ; the areas of focal fibrosis, as a series of dots.

ventricle in its middle and distal portions. Whereas the bulk of the infarct was subendocardial, this latter anterior portion moved away from the endocardium to lie intramurally.

This " sheet " infarct was of recent origin and was yellowish-red in colour. Its extent together with the areas of focal fibrosis are shown in Fig. 4. Comparison may be made with the distribution of the subendocardial fibres of the superficial bulbo-spiral muscle in Fig. 5.

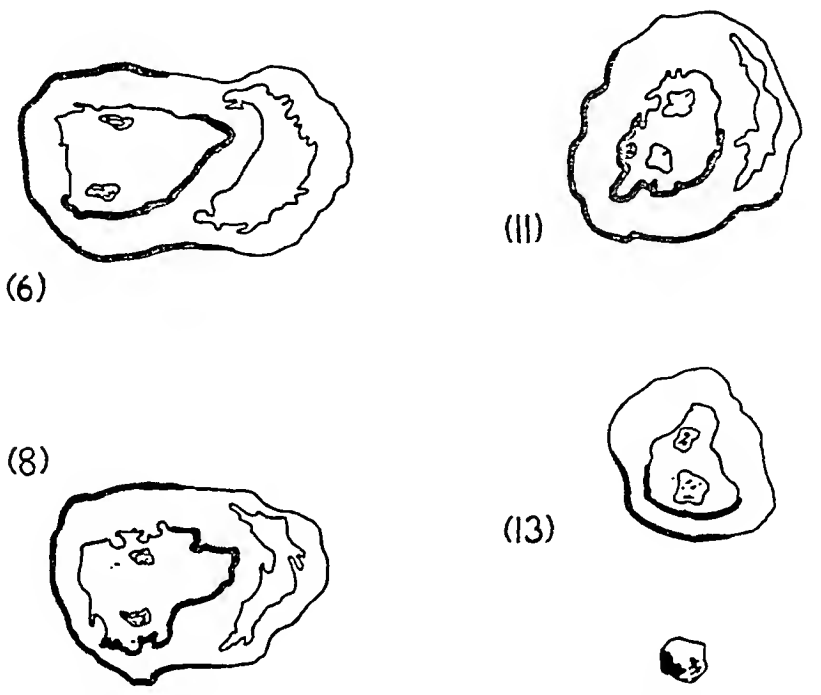
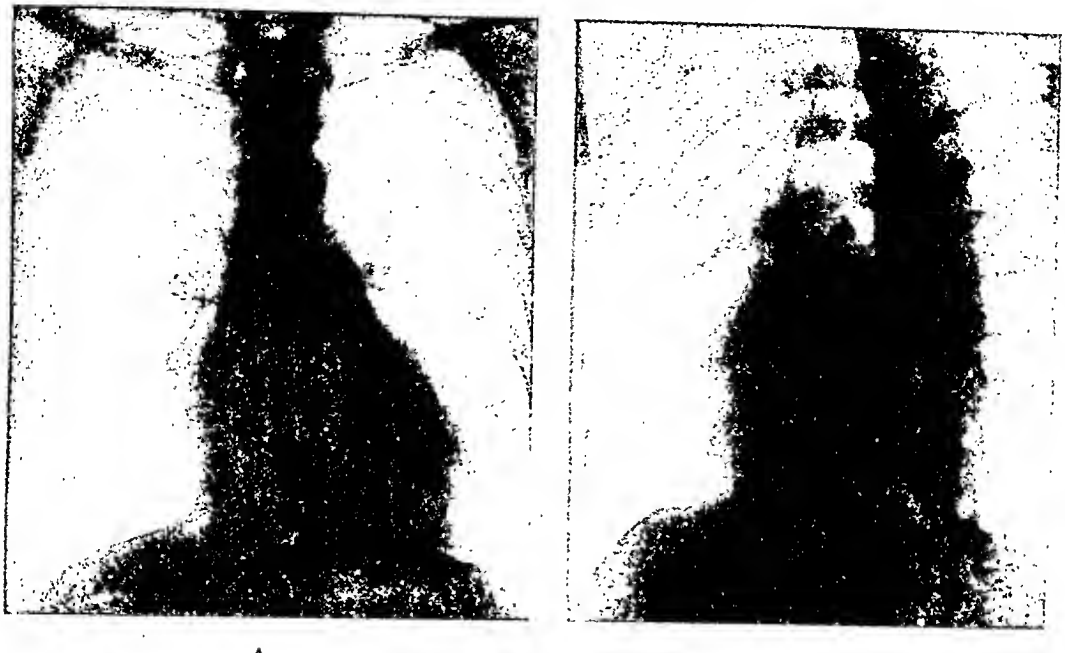


FIG. 5.—Photograph of a drawing to illustrate reconstruction of the superficial bulbo-spiral muscle. The numbers correspond approximately to the same level of transverse section as numbered in Fig. 4 [after T. E. Lowe (1939)].

DISCUSSION

A number of references to subendocardial infarction have been found. Parkinson and Bedford (1928) described occlusion of the circumflex branch giving rise to infarction of the lateral and posterior walls of the left ventricle usually involving the papillary muscles of the mitral valve. Whitten (1930) in an article on the relation of the distribution and structure of the coronary arteries to myocardial infarction mentioned one type of subendocardial infarct, which he suggested was due to occlusion of one or more of the large subendocardial branches that course often for a considerable distance in the subendocardial musculature, usually in relation to the columnæ carnæ or papillary muscles. Barnes and Ball (1932) investigated the incidence and situation of myocardial infarction in 1000 consecutive autopsies at the Mayo Clinic and found 49 cases, of which 28 were anterior apical, 24 posterior basal, 8 midventricular, and 3 diffusely beneath the endocardium; they state that in an occasional instance chronic infarction is diffuse, tends to extend in the form of subendocardial fibrosis and involves the entire left ventricle more or less completely. Lowe (1939) from a study of myocardial scars suggested a type of myocardial infarction that depends upon the interruption of the blood supply to a muscle bundle in the myocardium; this muscle bundle need not be supplied by a single main coronary vessel but may receive its blood supply from smaller branches of a number of vessels. In later articles, 1939 and 1941, he reported cases and attempted to correlate the clinical and cardiographic evidence with the post-mortem findings. Among the 5 new cases reported in 1941, Case 91 showed cardiographic changes consistent



A B

FIG. 1.

(A) 1938. Radiograph showing general enlargement of heart. In 1941 (one month prior to death) a radiograph showed no evidence of any increase in size since 1938.
(B) 1938. Left (11) oblique view showing left ventricular enlargement.

that his eyes were rather prominent and there was some clubbing of his fingers. Examination of the heart was as before with a blood pressure of 100/70. The thyroid gland was not enlarged or palpable. His basal metabolic rate was +48 per cent with a basal pulse rate of 92. On 17/5/41 he was first seen by us and a note was made: "Main complaint, loss of energy and marked sweating. On questioning, a cough for nearly two years with some sputum (this had been negative for tubercle bacilli in the past), never blood-stained. Weight constant. Some palpitation on exertion, no nervousness, fair appetite, had always had mild exophthalmos."

Examination showed no tremor but much sweating and marked nasal catarrh. No thyroid enlargement and no positive eye signs. Early clubbing of fingers. Heart enlarged. Moderate systolic murmur just internal to apex beat. Spleen not enlarged.

This time his metabolic rate was +60 per cent with a pulse rate of 80. X-ray of chest did not show any pulmonary infection and the heart shadow could be exactly superimposed on that taken in 1938. It was considered that surgery was not indicated at the time and observation was therefore continued and further attempts were made to control his diabetes and his excessive sweating. He was improving and the diabetes becoming more stable so that he was able to be about the ward helping with routine duties. A primary pituitary dysfunction explaining both the unstable diabetic state and thyrotoxic symptoms was considered possible. However, on 4/7/41 following seeing his visitors and being about to have his tea, with no symptoms of any sort, he went unconscious and died a few minutes later.

Post-mortem examination. This was carried out eighteen hours after death by Professor Haswell Wilson. The body was that of a well-developed man, with some lividity of the head, neck, and dependent parts.

The pericardial sac was normal. The heart (Fig. 2) was enormously enlarged, 1350 grams in weight. The left ventricle was hypertrophied, the wall measuring 5 cm. (after fixation in formalin). The right ventricle was also hypertrophied but to a much less extent, measuring 1 cm. in thickness. Both were slightly dilated with relative incompetence of the mitral and tricuspid valves. There was no ante-mortem thrombus. The coronary arteries were healthy in appearance but the solid mass of muscle showed areas of diffuse fibrosis, evidently a degenerative change supervening on extreme hypertrophy. There was no valvular lesion in the heart. The ascending aorta appeared to be of normal diameter at the aortic valves. The diameter gradually narrowed to a point just proximal to the attachment of the remnants of the ductus arteriosus. There did not appear to be any actual coarctation, the circumference at this point in the fixed specimen measured 5 cm. approximately. The distal part of the aorta tapered down gradually so that the circumference of the common iliacs

FIG. 2.—The interior of the left ventricle is shown. The great thickness of the wall and apparently normal aortic valves are seen. The right ventricle has also been opened and also shows hypertrophy (Case 1).

was only 2 cm. respectively. Extensive and severe atheroma was present in the lower part of the aorta and common iliac arteries, contrasting with the ascending aorta.

The lungs were voluminous and overlapped the pericardium. The left was adherent all over by old fibrous adhesions. The right was free. Both showed chronic bronchitis and emphysema, with sticky muco-pus in the bronchi and some œdema at the bases and posteriorly.

The peritoneum was normal. No abnormality was found in the abdominal organs. They were all engorged with blood. The pancreas showed no gross structural change.

The brain and its membranes were congested. The brain itself was rather atrophic with thin convolutions and wide perivascular spaces. The vessels at the base were healthy. No obvious lesion was found in the pituitary, thyroid, or suprarenals.

Histology. The heart muscle fibres were generally greatly hypertrophied although some were atrophic (Fig. 3). All sizes of fibres were present up to a diameter of 23μ. The nuclei were also markedly enlarged, appearing lobulated in many cases. Throughout the whole myocardium the interstitial fibrous tissue was increased and in some areas this was marked. There was no evidence of any inflammatory lesion. The arteries appeared normal though in several areas there seemed to be an increase in the perivascular lymphatic spaces of some arteries. There was no evidence of arteriosclerosis. Special stains did not reveal the presence of either amyloid or glycogen.

Sections from the thyroid and kidneys were entirely normal. Sections from the pituitary were not made.

Comment. This man was able to carry on heavy work as a foundry worker for at least two years with no increase in the radiological size of his heart. Only in the last year of his life did symptoms of diminished cardiac reserve appear. Moreover the measurement of the heart by X-ray examination gave us little indication of the excessive weight. The reason was obvious at autopsy when it was seen that the size of the heart chambers was small when compared with the muscle mass.

For some inexplicable reason the mode of death in gross enlargement of the heart is frequently sudden ; and pathological examination, as in this patient, is often unable to elucidate the actual cause.

NOTES OF SECOND CASE

A woman, aged 32, was admitted to the Birmingham United Hospital in August, 1939, for increasing shortness of breath and palpitation on exertion. She had been short of breath all her life, a

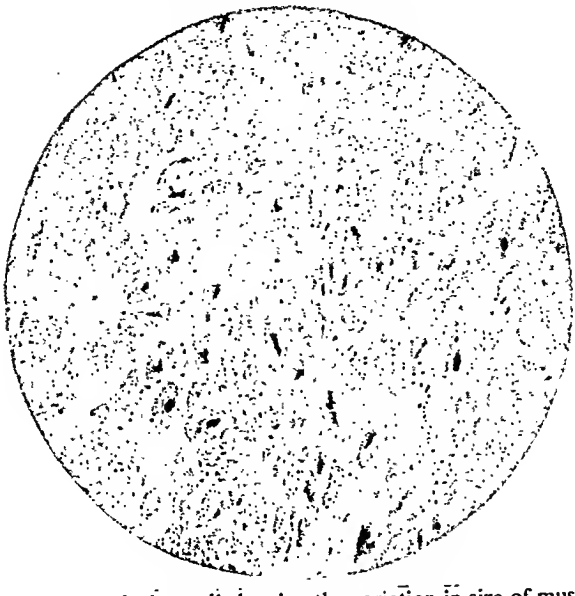


FIG. 3.—Photo-micrograph of ventricular wall showing the variation in size of muscle fibres and the increase of fibrous tissue. Magnification × 150 (Case 1).

fact she had attributed to a goitre. Her arms had always been hairy and her menstruation irregular. For ten years she had been taking thyroid tablets which caused her periods to become regular. Her weight had been constant at 165 lb. for many years. Recently her shortness of breath had become so marked that she was unable to do her housework and could only sit out of bed in a chair. Examination then showed a patient of masculine build, 5 ft. 8 in. tall, with a large head and hands and hairy arms and legs. The thyroid was enlarged, extending up from behind the sternum. There was no exophthalmos. The apex beat was outside the midclavicular line (Fig. 4): the heart was filbrillating

FIG. 4.—Radiograph of the chest (Case 2) showing the large retrosternal goitre, the enlarged heart, and the marked pulmonary vascular shadows, especially at the hila.

with a systolic and diastolic murmur at the mitral area heard all over the praecordium. The blood pressure was 130/80. There were no obvious clinical signs of congestive cardiac failure. The lungs, abdomen, and central nervous system did not show any abnormality. A cardiogram showed auricular fibrillation, rate 125, and left axis deviation.

An X-ray of the skull showed enlargement of the pituitary fossa. Her basal metabolic rate taken on five separate occasions varied between +21 and +28 per cent. A diurnal variation blood sugar curve showed values never rising above 100 mg. per 100 c.c. A diagnosis of acromegaly, retrosternal goitre, and rheumatic heart disease with mitral stenosis was made. Following a period of treatment with digitalis and Lugol's iodine, a subtotal thyroidectomy was carried out by Mr. Hugh Donovan in October. She made a satisfactory convalescence and was discharged home on the twelfth day after operation.

Histological report on the gland was as follows: "The gland is divided up by broad dense bands of fibrous tissue into lobules. The epithelium in these areas stains well and is slightly more prominent than usual. Colloid, however, is plentiful and only here and there exhibits a foamy appearance. The histological picture suggests that the thyroid hyperactivity is not a very marked feature."

At home she carried on normally until about one year prior to her final admission when she again became short of breath and unable to do her house duties. She became increasingly dull and disinterested, culminating in a refusal to speak. She was admitted to hospital for the second time in March, 1942. She was then uncooperative, incontinent, and in marked congestive failure (B.P. 105/80). She made no response to therapy. On account of her mental condition she was transferred to a mental hospital, where she died in congestive failure in May.

Post-mortem examination. This was carried out by Dr. Cox twelve hours after death. The body was well-nourished, with very large hands and feet and with marked ascites.

Very thick skull. Brain (1644 g.), normal externally except for small adhesions at tips of frontal and temporal lobes. Pituitary fossa very enlarged. Antra, chronic infected membranes. Frontal sinuses clear. Sphenoids, heavily infected. Teeth, septic and carious.

Lungs, normal in appearance and texture. Sero-sanguinous fluid in both pleural cavities.

Pericardial sac contained 1600 c.c. of straw-coloured fluid. Numerous pericardial adhesions.

Heart covered with thick white fibrinous membrane, the result of old pericarditis.

Heart: weight 900 g. Left ventricular chamber small with greatly hypertrophied walls, maximum thickness 30 mm. (Fig. 5). Right ventricle also hypertrophied but dilated, maximum thickness 8 mm. Left auricle dilated with some increase in the thickness of its wall. Right auricle also hypertrophied and dilated. In the posterior half of the interauricular septum, there was failure of development of the septum secundum, causing a septal defect 22 mm. in diameter. Chordæ tendineæ of mitral valve hypertrophied. The valve cusps themselves were normal as were those of the tricuspid, aortic, and pulmonary valves.

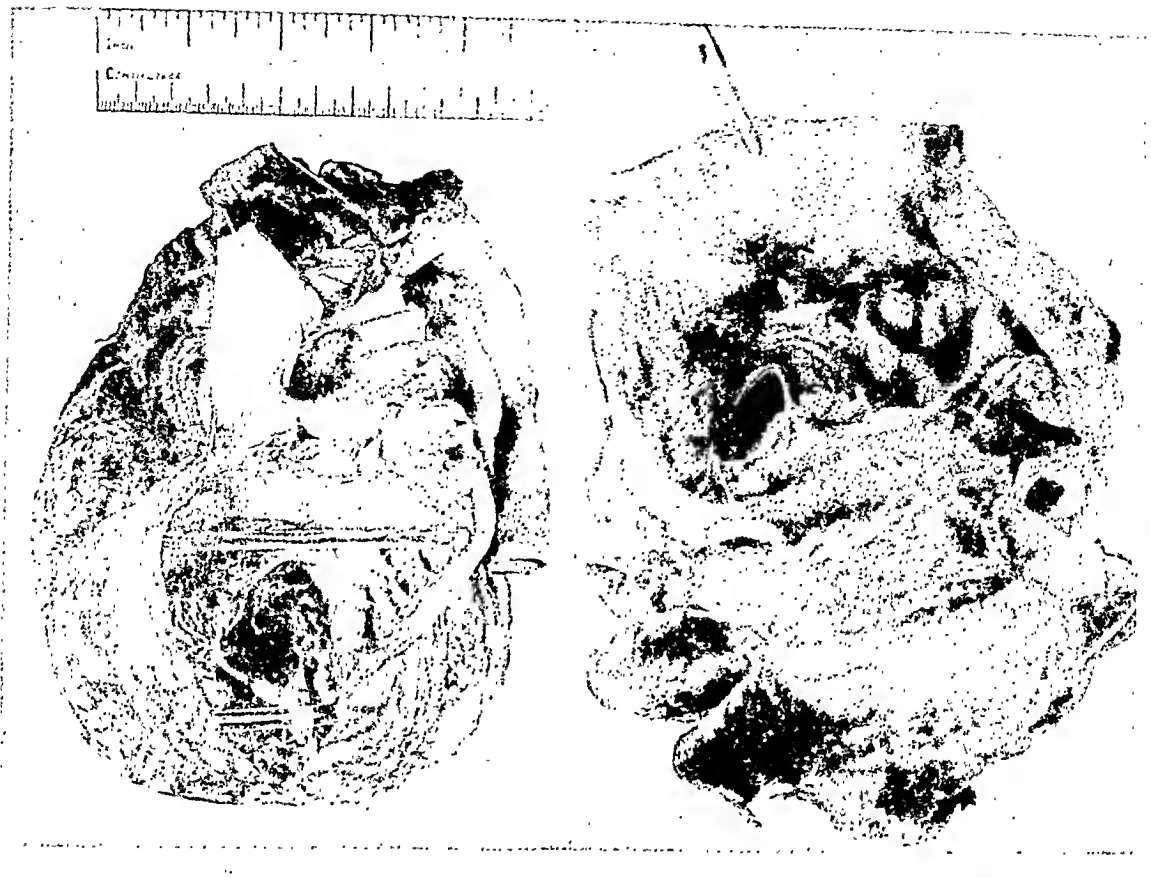
Pulmonary artery, enlarged. At the pulmonary valves, the circumference was 11 cm. Left pulmonary artery, 1 cm. after bifurcation, measured 9 cm. in circumference.

Aorta, hypoplastic, the circumference at the aortic valves being 8 cm.; at the level of insertion of the fibrous remnant of the ductus arteriosus, 6 cm.; and at a point 12 cm. distal to that, 5 cm. There was no atheroma. The pulmonary veins opened into the left auricle while the superior and inferior vena cava emptied into the right auricle.

Free fluid present in the abdomen. Liver (1990 g.) dark and congested. Spleen (164 g.) unusually firm. Kidneys: right (294 g.) normal; left (420 g.) large number of cysts at the upper pole, otherwise normal. Ovaries, large and fibrotic. Uterus, irregular with fibroids on the posterior surface.

Histology. Sections from the kidneys, liver, and adrenals were normal except for congestion. The heart muscle showed no evidence of inflammation. The individual fibres were large with normal nuclei. The pericardium was thickened with many layers of fibrous tissue, but no area of active inflammation could be detected. The pituitary showed poorly staining cells only. There was no adenoma or obvious increase of eosinophilic cells.

Comment. Enlargement of the heart is frequently noted in interauricular septal defect. For example, Roesler (1934) reported the case of a girl, aged 14, with a heart weighing 800 g., while Bedford, Papp, and Parkinson (1941) included in their series of 52 cases the case of a woman, aged 36, with a heart weighing 930 g., although this was associated with rheumatic heart disease and mitral stenosis. The enlargement and hypertrophy in such cases involves the right side of the heart, the left auricle and ventricle appearing sometimes almost as appendages. Commonly the pulmonary artery is much enlarged while the aorta is smaller than normal. In this case there was marked enlargement of the pulmonary artery and the aorta was small: the ratio between the two circumferences was essentially that given by Roesler, 3:2. The cardiac hypertrophy, however, did not involve the right side, throwing doubt upon the role of the septal defect in the production of such massive enlargement. This finding also suggests that the frequent association of septal defect with a small aorta is not always due to the diminished output of the left ventricle as was suggested by Bedford, Papp, and Parkinson.



A B

FIG. 5.—Photograph of the heart.

(A) The right ventricle is opened, showing some hypertrophy of its wall, the large pulmonary artery, and the comparatively small aorta.
(B) The dilated and hypertrophied left auricle is opened showing the interauricular septal defect.

Adhesive pericarditis has been noted in atrial septal defects by many writers, *e.g.* by Cossio and Arana (1937), and by Bedford, Papp, and Parkinson (1941), though usually in association with rheumatic valvular disease. The exact ætiology in this case is obscure though it was probably rheumatic. Auricular fibrillation is also common, occurring in 28 cases out of the 62 collected by Roesler; though Bedford, Papp, and Parkinson did not find any recorded case occurring below the age of fifty except in association with mitral stenosis. Finally, there was no evidence in this case that hypertension had been present to account for the enlargement of the left ventricle.

DISCUSSION

Enlargement of the heart usually takes place for two reasons only, either in response to increased work (*e.g.* high blood pressure, valvular disease, or arteriovenous aneurysm) or to the impairment of the heart's metabolism and reserve by rheumatic fever, the anoxæmia of coronary disease, or lack of thyroid hormone or vitamin B_1, etc. In Case 1, none of these intrinsic factors appeared to play any part. It is difficult to assess the role of diabetes with recurrent hypoglycæmia with subsequent impairment of function. It is not probable, however, that this factor caused such hypertrophy in the short space of two years, from the time of onset of his diabetes in 1936 to the time of the first X-ray in 1938. In Case 2, the role of the septal defect was probably small, seeing that the predominant hypertrophy affected the left ventricle, whilst there was no evidence of the presence of coronary disease, or of vitamin or thyroid deficiency.

Both large and small hearts may be found in aortic hypoplasia, while hypertrophy, usually attributed to the associated high blood pressure, is frequently found in coarctation of the aorta. This last condition occurs in varying degrees, from constriction that is scarcely recognizable to actual atresia, and may be associated with hypoplasia of the distal aorta, again of varying degrees. In Case 1, there did not appear to be any definite coarctation but there was a rapid diminution in the width of the aorta, commencing just proximal to the fibrous remnant of the ductus arteriosus. In Case 2, the aorta appeared to diminish gradually in size from the aortic valves themselves.

The role played by the narrowed aorta in the production of hypertrophy is obscure and there is very little to be gathered from other reports. The first description of aortic hypoplasia was that given by Morgagni in 1788. King (1841) drew attention to the condition in this country. On the continent, Virchow (1872), Spitzer (1897), Burke (1901), and Apelt (1905), all described cases associated with cardiac hypertrophy but none of them had any data on the blood pressure. Spitzer held that hypertrophy was found if the patient attained adult life; otherwise the heart would be smaller than normal. Virchow attributed the hypertrophy to the narrow aorta and increased elasticity of the vessels. In a number of these early cases changes were noted in the kidneys so that it is probable that high blood pressure was present in some. However, as Apelt pointed out, there was no constant feature in any case by which one could say hypertrophy would be present or not. More recently, Whittle (1929) reported the case of a young man, aged 20, who collapsed and died in the street; other than a recent attack of influenza, there was no record of any previous illness. The autopsy revealed a heart weighing 793 g., with a general enlargement chiefly affecting the left ventricle; the descending aorta was hypoplastic, but it was not specifically stated whether the thoracic aorta was of normal calibre; the remaining organs were normal though the heart was not tested for glycogen. Cluver and Jokl (1942) reported the case of an international Rugby football player who suddenly dropped dead. The arch of the aorta were of normal size but the abdominal aorta measured only half an inch, half the normal size; the heart weighed 482 g.; and the left kidney was the seat of advanced hydronephrosis and pyelo-nephritis. They called attention to the large thymus (26 g.) and the possible secondary effects upon the adrenal and pituitary glands.

It is difficult in the two cases here reported to explain the association of gross hypertrophy and normal blood pressure by any of the accepted physiological concepts. Eyster (1927 may provide some clue as to how such hypertrophy takes place. He showed that, by placing a constricting band around the aorta of dogs for a short period, hypertrophy followed some months later, and he suggested that the temporary dilatation provided the stimulus for the subsequent enlargement. This concept might be extended to these cases. The temporary dilatation to cope with the extra output requirements in strenuous work, might act as the stimulus for the hypertrophy and the finding of a normal blood pressure at rest.

While aortic hypoplasia may have played a large part, we find it difficult to believe that this factor alone would account for such massive enlargement. In Case 1, the heart was almost twice the weight of any of the other recorded cases. Case 2, however, was acromegalic and, in view of other recorded examples, *e.g.* Cushing and Davidoff (1927), and the general splanchnomegaly that occurs, it may be assumed that pituitary dysfunction played a large part in the production of the cardiac hypertrophy. Amsler (1912) attributed such hypertrophy to a direct hormonal action on the heart, while Courville and Mason have reported two cases suggesting that enlargement of the heart may precede the development of obvious signs of acromegaly. They stressed the high incidence of hypertrophy and heart failure and the infrequency of high blood pressure in acromegalics, and concluded that the hormonal theory offered the most satisfactory explanation for the cardiac enlargement.

In Case 1, the very variable response of the diabetes and the symptoms suggestive of thyrotoxicosis were clinical features that pointed to a primary pituitary defect. Therefore, if only

for the sake of directing future observations to the possibility in obscure cardiac hypertrophy, we would suggest that excessive action of the anterior lobe of the pituitary gland may have played a part in producing the extreme enlargement found in this patient. Unfortunately, owing to an oversight, no sections were made of the pituitary gland.

Finally, we can only agree with Sir Thomas Lewis (1933) that "There is still much that remains to be explained: it is clear that there must be hidden sources of increased work or the conclusion that increased work is the cause of hypertrophy needs revision."

Summary

Two cases of extreme cardiac hypertrophy are reported.

In the first, a male diabetic, aged 33 years, the heart weighed 1350 grams. There was no associated valvular disease and only moderate increase in the size of the heart chambers. The descending part of the thoracic and abdominal aorta showed moderate hypoplasia. No definite cause for this extreme cardiac hypertrophy could be found, but there was evidence of thyrotexicosis and it is suggested that pituitary hyperfunction played some part.

In the second, a female acromegalic, aged 35 years, the heart weighed 900 grams. The hypertrophy affected the left ventricle predominantly and was associated with an interauricular septal defect and hypoplasia of the aorta. The pituitary dysfunction was thought to have played the chief part in the production of the enlargement in this case.

We are indebted to Professor Haswell Wilson for the pathological report of Case 1, and we wish to thank Dr. Oscar Brenner for the clinical details, Dr. Pickworth and Dr. Cox for pathological and microscopical reports in Case 2, and Dr. T. C. Graves, Medical Superintendant, Rubery Hill Hospital, for facilities granted.

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EISENMENGER'S COMPLEX

BY

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An opening at the base of the interventricular system in association with other defects is one of the commonest of congenital cardiac lesions. The usual combination is Fallot's tetralogy, which consists of a ventricular septal defect, dextraposition of the aorta, and stenosis of the pulmonary artery, with cyanosis.

A much rarer condition is that known as the Eisenmenger complex, where dilatation of the pulmonary artery occurs instead of stenosis, together with dextra-aorta and septal defect. This condition was originally reported by Dalrymple in 1847. Eisenmenger (1897) presented the first complete study of such a case, in which the diagnosis had been made during life by his colleague, von Schrotter.

In 1927, Maud Abbott described 8 cases, 3 of which she had studied personally. According to Baumgartner and Abbott (1929) the condition can be differentiated clinically from Fallot's tetralogy by the following points :—

(1) absence of, or only a moderate degree of clubbing and cyanosis,
(2) the localization over the præcordium of a harsh systolic murmur at the defect, not transmitted into the vessels of the neck,
(3) the occasional presence of a diastolic murmur of pulmonary insufficiency, and
(4) the distinctive character of the X-ray picture.

Hoarseness and aphonia, from pressure of the huge pulmonary conus on the recurrent laryngeal nerve, sometimes occur. Pulsation of the dilated pulmonary artery may be felt, and abnormal dullness percussed at the left base. The midsternal systolic murmur of the Eisenmenger complex is transmitted downwards to the right and to the left, as well as through to the back, whereas in the Fallot tetralogy it is usually transmitted upwards into the neck vessels and through to the back.

Polycythæmia, varying from 7,000,000 to 12,000,000 red cells, is a feature of Fallot's tetralogy, but not of the Eisenmenger complex.

Case Report

A male, aged 15, had been a " blue baby " at birth in 1928, and was troubled with his chest in infancy and childhood. He always had a high complexion and frequently had a bleeding nose ; he was breathless on exertion.

There was nothing of interest in the family history.

During the period 1934–1937 he was in hospital three times with an exacerbation of his chronic bronchitis, complaining of præcordial pain on exertion, a hard dry cough, and attacks of respiratory embarrassment at night. A diagnosis of congenital pulmonary stenosis was made, and in 1937 a poor view was taken of his prognosis. Arrangements were made for his reception in a hospital for incurables ; but on arrival there with his mother he created such a disturbance that he had to be taken home : he had always been a noisy and obstreperous patient.

In 1943 the lad, now 15 years old, was seen during the course of a routine follow-up. His general health had been much better since his discharge from hospital, and he now led a very active life, although inclined to be troubled by bronchitis during the winter months. He no longer suffered from epistaxis or from præcordial pain, but sometimes took a stitch in the side when he " hurried up hills."

On examination he was small for his age but powerfully built. There was a tinge of cyanosis in the cheeks and lips, but no clubbing of the fingers. The pulse was regular in time and force, the rate 80, and the wave of good volume and well-sustained. His blood pressure was 110/80.

The left side of the chest was a little more prominent than the right, and there was diffuse pulsation in the fourth, fifth, and sixth interspaces. The apex beat was felt in the sixth space, four and a half inches from the mid-sternal line. It was diffuse and forcible. A thrill was palpable at the base, the point of maximum intensity being in the third left interspace just lateral to the border of the sternum. On percussion both the right and left borders of the heart were greatly enlarged, and the dilated pulmonary artery could also be made out, the dullness in the second left interspace extending two inches from the mid-sternal line.

On auscultation the predominant feature was a systolic murmur. It was best heard at the point of maximum intensity of the thrill but was audible all over the præcordium. It was mainly conducted downwards to the right and to the left, and through to the back, but was not heard in the neck vessels. The pulmonary second sound was inaudible beneath the prolonged systolic murmur in this area, but a distinct diastolic murmur could not be distinguished. In the aortic and mitral areas the second sound was pure and closed.

No evidence of recurrent laryngeal involvement could be found. There was an undescended testicle on the right side. Blood examinations had been carried out on various occasions, the red count varying from 5·2 to 5·5 million, and the hæmoglobin from 108 to 116 per cent. The Wassermann reaction was negative.

The chief features on X-ray examination were (*a*) great enlargement of the right ventricle, (*b*) no demonstrable enlargement of the left auricle, (*c*) a right-sided aortic arch, displacing the œsophagus forward, and (*d*) prominence of the pulmonary artery (Fig. 1 and 2).

The chief features of an electrocardiogram in 1934 were a normal sinus rhythm with runs of complete dissociation, and right axis deviation (Fig. 3). A record in 1941 showed disappearance of complete dissociation. There was an increase in the height of the P waves in

FIG. 1.—Radiogram showing hypertrophied right ventricle, dilated pulmonary artery, and dextra-aorta.

FIG. 2.—Left (II) oblique position, showing forward displacement of the œsophagus by the right-sided aortic arch.

leads I and II. The QRS interval had increased from 0·06 to 0·12 sec. Inverted T waves had developed in leads II and III, and an S–T depression in lead II. The sternal lead showed depression of S–T, and a diphasic T, while there was a steep inversion of the T wave in

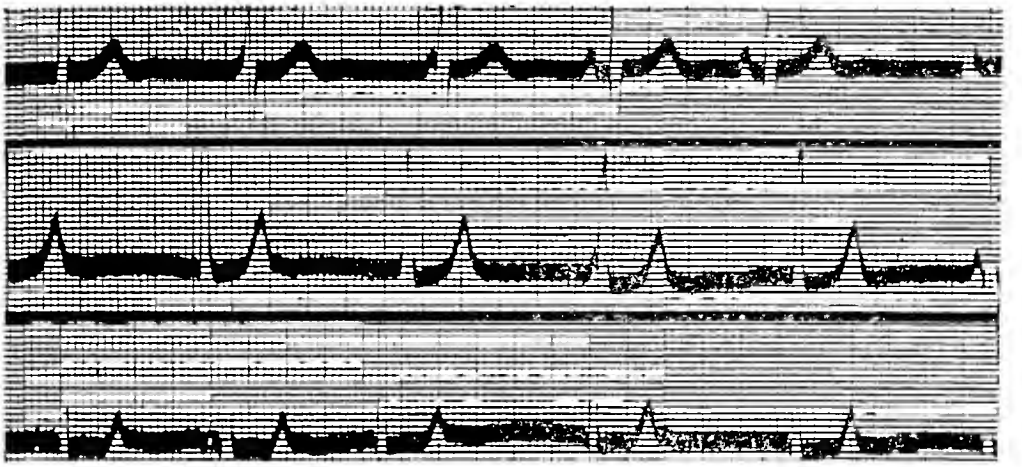

FIG. 3.—Cardiogram taken in 1934, showing right axis deviation and runs of complete dissociation.

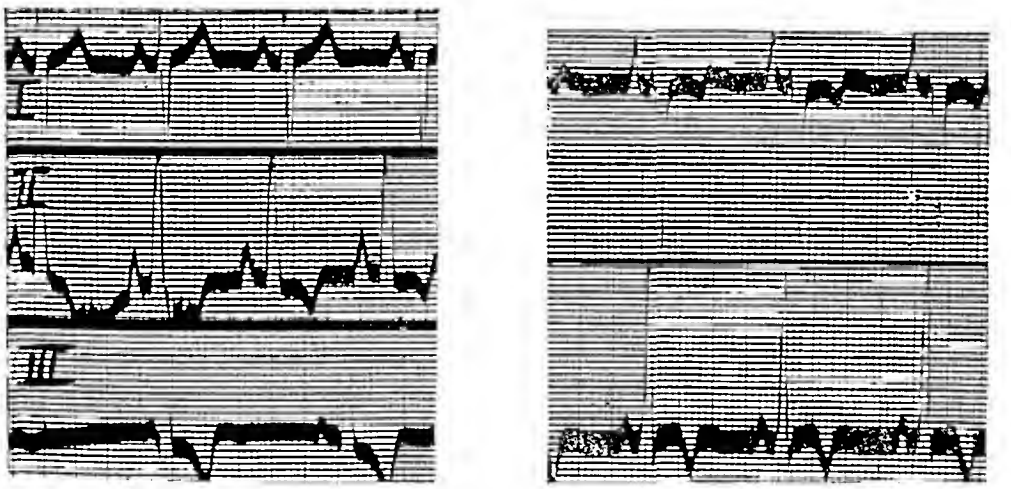

FIG. 4.—Cardiogram taken in 1943, showing larger P waves, especially in lead II, and (usually) normal rhythm. On the right ; sternal C_2F above, and apical C_4F below.

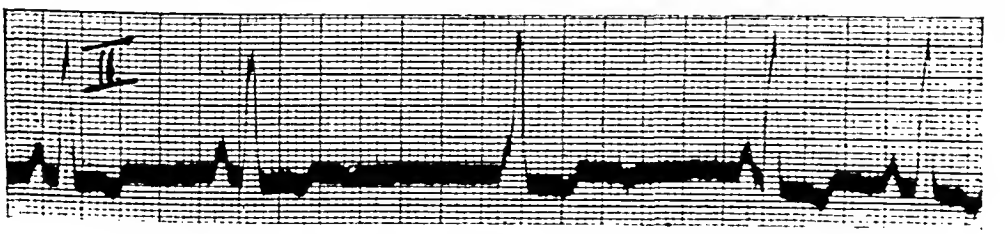

FIG. 5.—Cardiogram taken in 1943, showing occasional dissociation.

the apical lead. In 1943, little further change was recorded (Fig. 4). Infrequent runs of complete dissociation could be made out (Fig. 5), but normal sinus rhythm predominated.

Aetiology

According to the theory of Spitzer (1923) so enthusiastically endorsed by Maud Abbott in her monograph, the critical period of heart formation lies between the fifth and eighth weeks of embryonic life, i.e. before the cardiac septa are formed. During this time, the complex processes of torsion, involution, re-adjustment, and fusion, necessitated by the development of the heart from a simple tube to a four-chambered structure, are taking place. The appearance of the heart in the tetralogy of Fallot is highly suggestive of the relationships that would result from the uncovering of the right reptilian aorta and the obliteration of the left, in the delayed torsion of Spitzer's theory.

The dilatation of the pulmonary artery in the Eisenmenger complex has been attributed to inflammatory lesions. Thus in Blechman and Paulin's case (1922) a streptococcal endarteritis was thought to be the cause of the dilatation. In Stewart and Crawford's case (1933) the histology of the pulmonary arteries suggested an inflammatory process. The authors gave reasons for ascribing the inflammation to a syphilitic infection, but their evidence was based purely on the histological appearances. In their case they found also an old healed endocarditis of the pulmonary valve, and in addition atherosclerotic changes in the pulmonary arteries. They suggest that the syphilitic infection might have been congenital and the chief cause of the cardiac anomalies, and that the pulmonary dilatation was quite possibly due to the arteritis.

Taussig and Semans (1940) describe a case of Eisenmenger's complex in a negro, aged 7 ; a healed lesion of the aortic valve was present, the extensive fibrosis and hyalinization showing it to be of long standing : they question whether the lesion was the result of healed bacterial endocarditis, or really related to the congenital malformation.

Inflammatory changes are frequently found in association with abnormal blood streams in the heart. Thus in *Maladie de Roger* sub-acute endocarditis commonly occurs around the margins of the septal defect and upon the wall of the right ventricle opposite the defect (Abbott, 1936). Moschcowitz (1914) described active non-rheumatic vegetations in congenital heart disease, and according to Boldero and Bedford (1924), the determining factor seems to be the access of arterial blood to the right side of the heart.

The balance of evidence is in favour of the view that the inflammatory lesions in the right circulation arise primarily as a result of the congenital abnormality. That they were so marked and widespread in Stewart and Crawford's case is no doubt related to the advanced age to which this patient lived (60 years).

The pulmonary dilatation and atherosclerosis are more simply explained as a sequel of the increased pressure in the right heart. Certainly in cases of septal defect only, very great dilatation of the pulmonary arteries may occur, with subsequent pulmonary fibrosis and the production of Ayerza's disease. Such dilatation cannot take place in Fallot's tetralogy, owing to the deformity and constriction of the lower pulmonary bulbar orifice.

Prognosis

The prognosis in these cases is the only point of practical clinical interest. The pulmonary stenosis of the Fallot type forces a good proportion of the venous blood to enter the overriding aorta. This causes the cyanosis, the polycythæmia, and the very marked clubbing. The combination of defects is obviously a very serious one, and the average life is 12 $^3/_4$ years, although Paul White's case (1929) attained 59 years.

In the Eisenmenger type of anomaly, the dilatation of the pulmonary artery does not hinder the entrance of venous blood into the lungs. The shunt normally takes place from left to right and little mixture of venous and arterial blood occurs. Clubbing and cyanosis are therefore slight or absent, and polycythæmia is not a feature.

The prognosis is rather better than in the Fallot type, and the average life is 16 years.

Stewart and Crawford's case (*loc. cit.*), in spite of hard living, reached 60 years, untroubled by his cardiac abnormality.

The lad described in this paper presents all the clinical features of the Eisenmenger complex, and the X-ray examination supports the diagnosis. Although he had a stormy childhood, much troubled by bronchitis, in recent years his health has been much better. At his present age of 15 he leads a very active existence, and refuses to consider any curtailment of it. Rising at six every morning, he does a paper round before going to school. In his spare time he takes his full share in the activities of his group of boy scouts, joining in their physical training, their rough games, and their week-end hikes.

Summary

A case presenting the clinical and radiographic features of the Eisenmenger complex is described, and the ætiology and prognosis briefly discussed.

I have to thank Professor D. M. Lyon for his help and advice.

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CASUAL AND BASAL BLOOD PRESSURES
I.—IN BRITISH AND EGYPTIAN MEN

BY

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In the course of clinical investigations on healthy Egyptian men, we observed that during a period of rest in the sitting posture the systolic blood pressure often fell below 90 and usually below 100 mm. of mercury. This led to a study of the blood pressures of British subjects resident in Egypt and of others resident in London. The pressure found under the conditions described below is called basal* blood pressure because it was not found possible to reduce it appreciably below this level by rest or sleep. Our observations in a physiological type of low blood pressure may be of interest in relation to low blood pressure which is thought to be pathological.

METHOD

Measurements of the blood pressure were made by the auscultatory method, either with manometers in which the whole of the mercury column was visible, or with those of the Baumanometer type which had been checked by an ordinary mercury manometer. The diastolic pressure was taken at the moment when the arterial sound becomes muffled, usually 5 mm. higher than that at which the sound disappeared. The blood pressure was measured on the left arm with the subject sitting in a quiet, warm room. All subjects were instructed to find a comfortable posture, and then to remain still and with the mind blank throughout the half-hour or longer period during which the measurements were made. No conversation was allowed. The observer avoided unnecessary movement, and as a rule no third person entered the room during this time. To allay apprehension the subjects were informed that the investigation would be confined to the repeated measurement of blood pressure. Most subjects became somnolent but in general did not sleep.

The blood pressure was measured as frequently as possible during the first three minutes after adopting the sitting posture. Blood pressure readings were then taken every few minutes throughout the half-hour period of rest, in order to habituate the subject to the procedure of blood pressure measurement. Without habituation of the subject by the continuous presence of the observer and by repeated measurements, the blood pressure falls are less than those we report. Towards the end of the half-hour period the measurements of the blood pressure were made at intervals of about one minute.

RESULTS

In Fig. 1 are recorded systolic blood pressures and in Fig. 2 diastolic pressures. The height of a patient's blood pressure, under the stated conditions, is indicated by the distance of the cross from the left-hand side. For each subject three systolic and three diastolic pressures are recorded in the diagrams, namely:

* The term "basal blood pressure" has already been used in the Joint Report of the Committees appointed by the Cardiac Society of Great Britain and Ireland and the American Heart Association, on the Standardization of Methods of Measuring the Arterial Blood Pressure. "In detailed researches on blood pressure the use of a basal pressure might be considered after preparation similar to that used for basal metabolism. It should be determined 10–12 hours after the last meal of the previous night, and after resting half an hour in warmed room."—EDITOR.

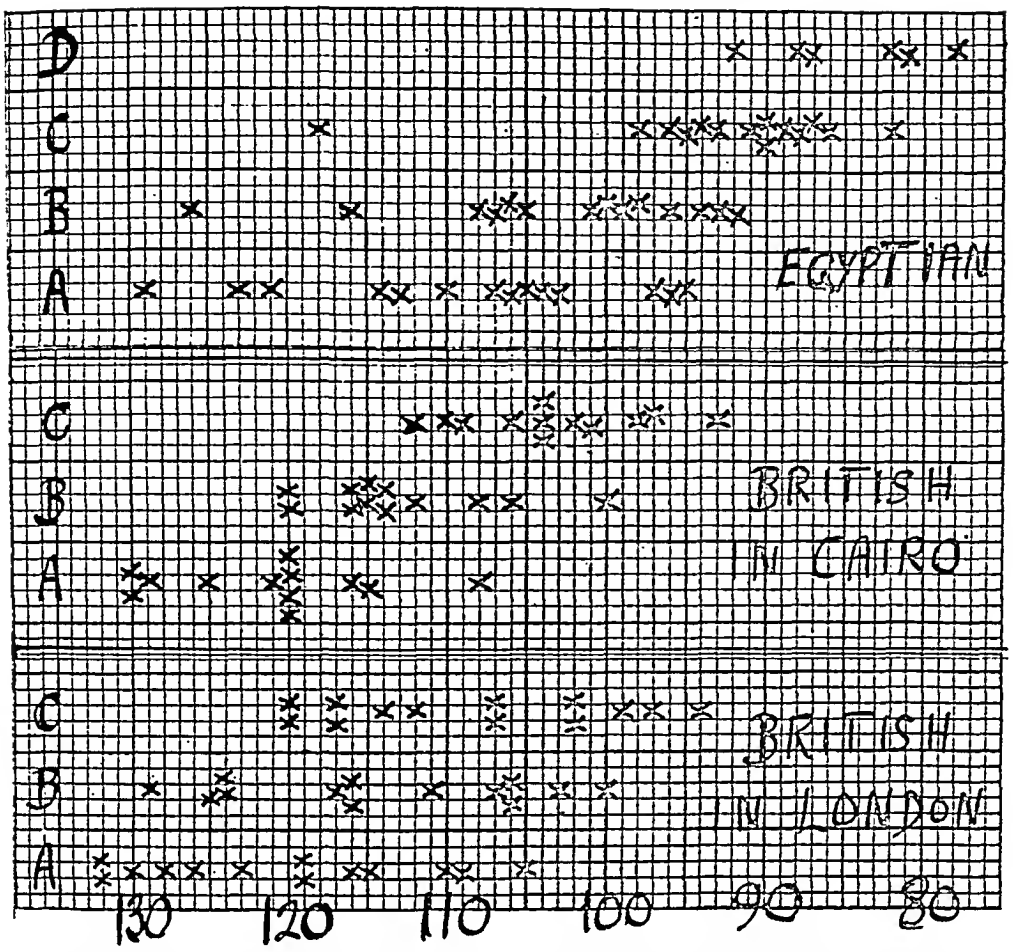

FIG. 1.—Effect of rest and emotional desensitization on the systolic blood pressure in 14 Egyptian nationals (above), in 12 British in Cairo (middle), and in 13 British in London (below). (A) Casual blood pressure. (B) Lowest pressure of the same subjects during the next 3 minutes. (C) Lowest level maintained for three consecutive readings during 30 minutes. (D) Level attained after 90 minutes. Details of the procedure followed during this period are set out under " Method."

(A) The casual blood pressure, which was measured soon after the patient entered the room and was seated;

(B) The lowest pressure measured in the next three minutes; and

(C) The basal blood pressure, which was the lowest level of the blood pressure that was maintained for three consecutive readings during the half-hour period of rest and habituation of the subject to the presence of the observer and to the procedure of blood pressure measurement.

The average levels of the systolic and diastolic pressure do not differ appreciably in the two British groups, but there is an evident difference between these and the Egyptian group. Casual blood pressures are lower and basal pressures are much lower in Egyptian nationals, approximately half the basal systolic pressures lying between 80 and 90 mm., and half the diastolic pressures between 50 and 57 mm. (Fig. 1 and 2).

The blood pressure measurements on British nationals in London were made during a hot, moist August. The pressures of British residents in Egypt and of the Egyptians were measured in Cairo, mostly in April and May, with a higher temperature and lower humidity than London in August. The Egyptian subjects referred to above were of the poorer classes, but the low pressures encountered were not due to malnutrition, since equally low pressures were observed also in well-nourished Egyptian students and doctors of a similar age group. These observations are supported by a considerable number of blood pressure readings made

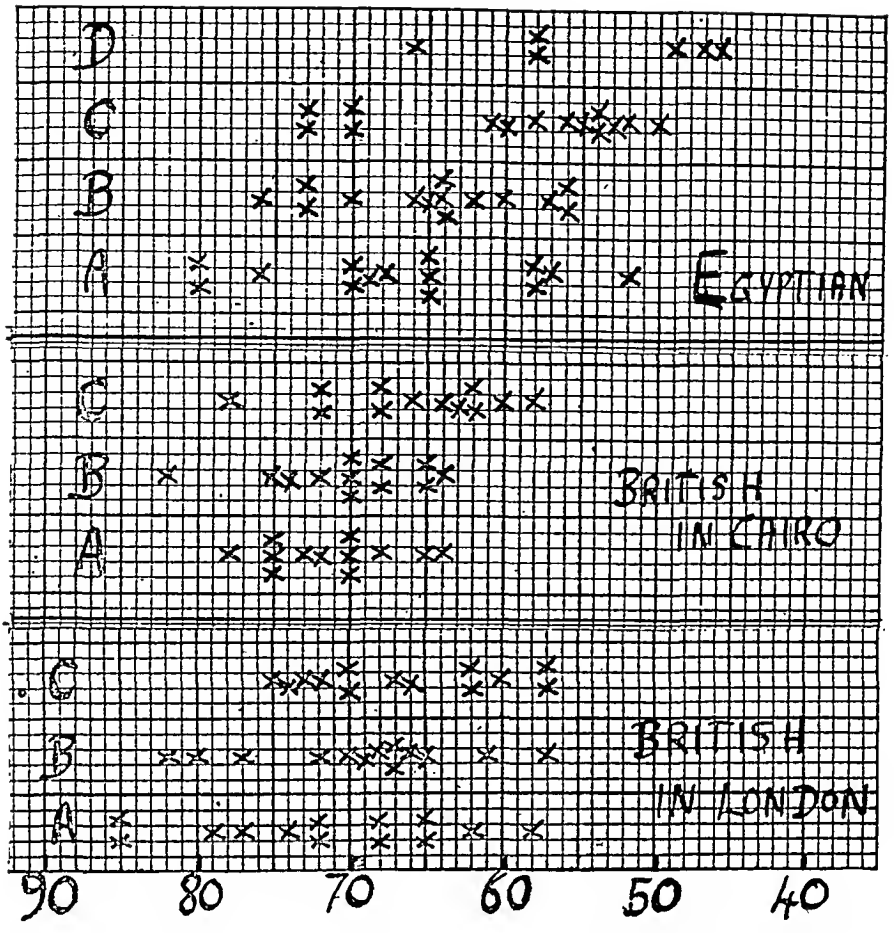

FIG. 2.—Effect of rest and emotional desentitization on the diastolic blood pressure in British and Egyptian nationals. (A), (B), (C), and (D) as in Fig. 1.

in the course of clinical investigations on patients without disease of the cardiovascular system. There seems no doubt that, under comparable conditions, both richer and poorer classes of Egyptians, whether heavy meat eaters or vegetarians, have lower blood pressures, especially basal pressures, than the British, and this difference is not explained to any great degree by the character of the food or by other differences in the environment. Arterial hypertension is, nevertheless, a frequent condition among in-patients in Egyptian hospitals.

The average of the casual blood pressures and of the basal blood pressures in young British and Egyptian nationals are set out in Table 1.

TABLE I

	Number studied	Average Blood Pressures	
		Casual	Basal
British	25	121/71	106/67
Egyptian	14	110/66	91/59

DISCUSSION

It is well recognized that the blood pressure is variable and is raised by emotion. In the many statistical studies concerned with the level of the blood pressure in health the figure recorded is for the casual blood pressure, in that usually few precautions are taken to guard against the pressor effects of emotion.

The normal European systolic pressure during sleep is of the order of 95 mm. of mercury (Müller, 1921; Brooks and Carroll, 1912). Some of the above observations were made during natural sleep, and in others sleep was induced by hypnotics such as sodium barbitone. In British subjects, the average basal systolic blood pressure with the subjects awake is about 106, which is 5 to 10 mm. higher than the reported average levels of the systolic pressure attained after some hours of sleep. If the patients fell asleep during the investigation no appreciable difference between the waking and sleeping pressures was noted. The possibility that the blood pressure falls further if sleep continues has not been studied. In a few Egyptians the measurements of blood pressure was continued for a period of three hours and further falls of blood pressure occurred; in five out of six the systolic blood pressure fell below 90 and in one to 78; in no case did any symptom develop.

The observer and his sphygmomanometer represent a stimulus that raises the blood pressure, and emotional habituation to both is required before a low level of the pressure is obtained. There is a widespread recognition of the variability of the blood pressure in health, and it is commonly stated that the figure which should be recorded is the lowest attained under conditions of rest. The pressures usually recorded under conditions of rest lie, with few exceptions, within the range of what is commonly regarded as normal. A considerable proportion, however, of our measurements made in healthy subjects at rest but with deliberate emotional desensitization, fall to levels commonly thought to be pathological (below 110–100, according to various authors).

In general, basal blood pressures cannot be obtained by repeated measurements made in a hospital ward, with or without screens about the bed; nor in subjects who suspect that the blood pressure measurements are only a prelude to further procedures. The environment of the subject must be entirely unstimulating. Restlessness on the part of the observer, noises outside the room, and displays of medical equipment may invalidate the result. In other words, observations on man require experimental conditions similar to those which Pavlov (1927) found essential in his conditioned reflex experiments on dogs. Emotional desensitization of the human subject by continued repetition of the stimulus and avoidance of new and especially of unfamiliar stimuli, bears a close resemblance to some of the experiments of the Pavlov school on conditioned inhibition in the dog.

Sometimes the blood pressure fell to a level which, encountered in surgical shock would indicate a dangerous condition. Under physiological conditions such low blood pressure is rarely observed with casual measurements. The difference between the casual and basal blood pressures varies considerably with different subjects. It may well be that many patients considered to be examples of hypotension have a normal basal blood pressure, but sub-average degrees of elevation of the casual above the basal pressure.

Summary

Egyptian men resident in Egypt have much lower blood pressures than British men resident either in Egypt or in England. This difference does not depend upon differences of temperature, diet, or social status.

Half an hour of rest in the sitting posture, together with deliberate emotional desensitization to the presence of the medical examiner and to the procedure of blood pressure measurement reduced the systolic blood pressure to below 100 in 13, and to below 90 in 5 out of 14 Egyptian men ; and to below 105 in 13, and to below 100 in 6 out of 25 British men.

Such lowering of the blood pressure was not associated with any symptoms.

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CASUAL AND BASAL BLOOD PRESSURES
II.—IN ESSENTIAL HYPERTENSION

BY

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The casual and basal blood pressures were determined in 27 Egyptian patients with essential hypertension, using the method described in the previous paper. Consideration has been given to the practical value of such measurements and to their bearing on the functional pathology of essential hypertension.

Results and Discussion

In half-hour periods of observation it was noted that physical and mental rest and habituation to the presence of the observer and his sphygmomanometer led to falls of blood pressure in essential hypertension greater than those which occur in health (Fig. 1 and 2). Thus in half-hour periods the average fall of systolic pressure in 14 healthy Egyptian subjects was 15 mm. of mercury, but in 13 Egyptian patients with essential hypertension (average systolic blood pressure about 200 mm.) the average fall of systolic pressure was 36 mm. The diastolic blood pressure in essential hypertension also exhibited a fall which was greater than that encountered in healthy subjects, being 18·5, as against 6·5 mm. in health.

In both hypertensive and healthy subjects further decreases in pressure could be obtained

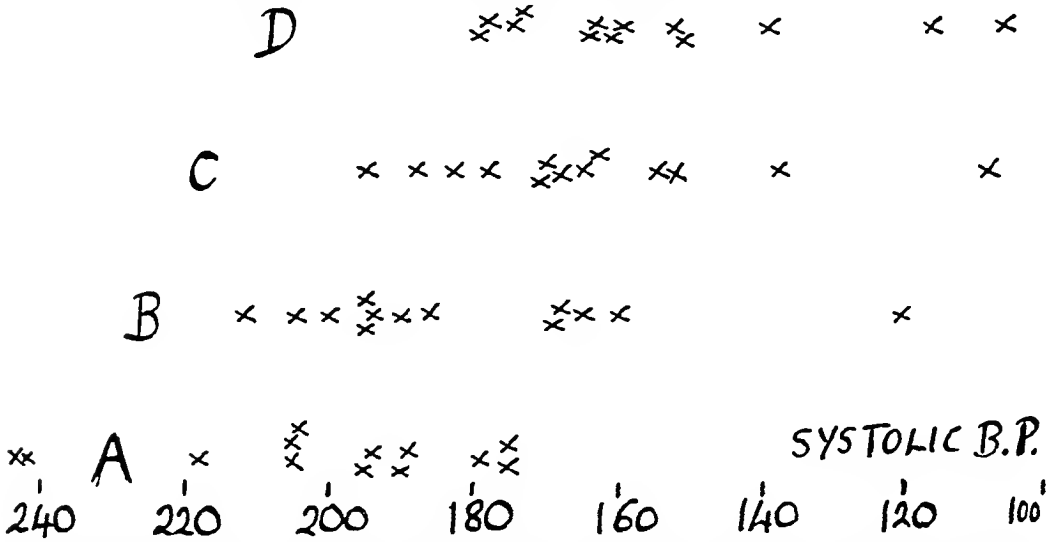

FIG. 1.—Effect of rest and emotional desensitization on the systolic blood pressure in essential hypertension (Egyptian nationals). (A) Casual blood pressures of 13 subjects with essential hypertension. (B) Lowest pressures of the same subjects during the next three minutes. (C) Lowest level maintained for three consecutive readings during half an hour. (D) Level attained after 2–4 hours. Details of the procedure followed during this period are set out under "Method."

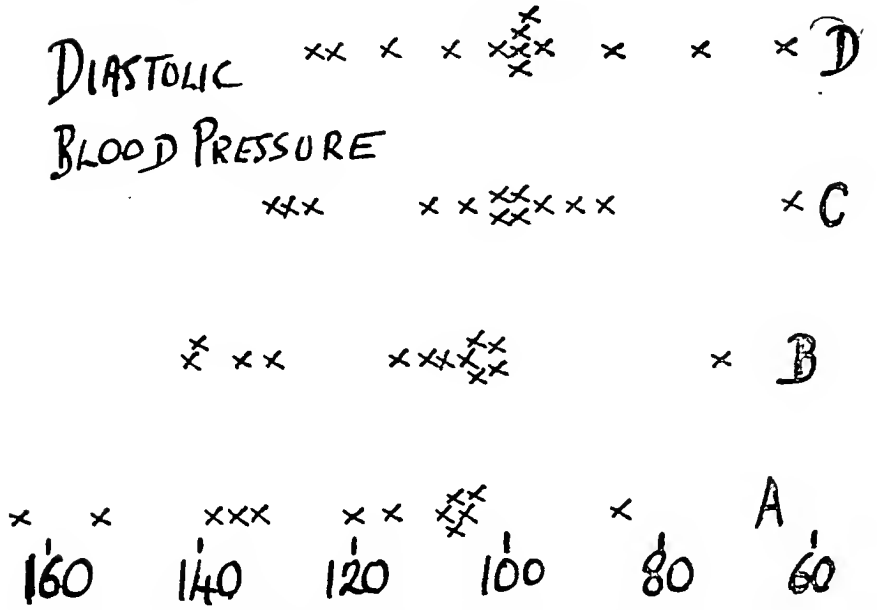

FIG. 2.—Effect of rest and emotional desentitization on the diastolic blood pressure in essential hypertension (Egyptian nationals). (A), (B), (C), and (D) as in Fig. 1.

by extending the period of rest to between 2 and 4 hours. In 27 patients with essential hypertension (including the 13 mentioned above) the average casual systolic pressure was 195 and the average pressure after 2–4 hours rest and habituation to the process of blood pressure measurement was 151. The average casual diastolic pressure was 116 and the average basal diastolic pressure 95. The systolic pressure fell to 77 per cent of its initial level and the diastolic pressure to 82 per cent. It would appear that in essential hypertension a period of about two hours rest and habituation to the process of blood pressure measurement is required before basal readings of the blood pressure are obtained.

In the course of our measurements patients occasionally fell asleep. In sleep of short duration the blood pressure did not fall appreciably below the basal level recorded with the subject awake. This observation and comparison of our basal blood pressure readings with those recorded during sleep by various authors (Brooks and Carroll, 1912; Müller, 1921), suggest that we are probably justified in describing the measurements we have made as basal pressures, since the blood pressure taken with the patient awake does not differ greatly from the blood pressure during the first few minutes of sleep.

The basal blood pressure cannot be guessed from knowledge of the casual blood pressure. In two patients each with casual systolic blood pressures of 195 mm. the basal blood pressures after two hours were 160 and 130 mm. One exceptional patient (European) had a casual systolic pressure of 290 with a basal systolic pressure of 130. It seems probable that the basal blood pressure is a fair indication of the resistance to contractions of the left ventricle during the hours of sleep, and that, in general, the work of the heart will be less for the lower basal pressure. The basal blood pressure may, therefore, be of assistance in determining prognosis.

It is common knowledge that in patients with essential hypertension the blood pressure usually falls appreciably during the stay in hospital. Physical rest in hospital is accompanied by familiarity with and emotional desensitization to procedures such as blood pressure measurement. Nevertheless, the lowest readings of the systolic pressure recorded casually in the wards are much higher than the blood pressure which may be attained in half an hour by the method we have used.

Much of the difference between casual and basal blood pressure is of mental origin, as is indicated by the following observations. In four patients with essential hypertension the

blood pressure was reduced to its basal value by rest and habitation to the presence of an observer, called observer 1, using the method described in the previous paper. Observer 2 then entered the room, conversed with the patient, and measured the blood pressure. The visit of observer 2 corresponds to an ordinary contact between doctor and patient; although a basal level of the blood pressure had been secured by observer 1, the pressure did not remain basal in the presence of observer 2. The blood pressure readings obtained by observer 2 were in all cases nearer to the casual than to the basal blood pressure. It was immaterial in this investigation which of the authors played the part of observer 2. Similar observations have been made on healthy subjects but with less striking pressure differences It appears therefore that in health and essential hypertension the difference between the levels of the basal and casual blood pressures depends to an appreciable degree upon the mental processes of the patient. Probably the difference is due to the stimulation of vasomotor nerves, but might be explained by the liberation of a vasoconstrictor substance. If, however, the liberation of a vasoconstrictor substance is responsible for the degree to which the casual blood pressure is higher than the basal blood pressure, then the substance is unlikely to be either adrenaline or posterior pituitary hormone, since amounts of these sufficient to influence the blood pressure appreciably cause striking pallor.

Fishberg (1939) refers to an interesting case of hypertension resulting from an emotional state, described by Mueller (1922), in which elimination of some domestic friction led to a fall in the systolic blood pressure from 280 mm. to 150 and finally to 130 mm. In the course of our investigation we had three experiences that indicated how adverse emotion may make it impossible to obtain a true basal level of the blood pressure. During this investigation, one of our collaborators arranged to administer a general anæsthetic to some of our patients with essential hypertension, partly with a view to determining their suitability for surgical treatment and partly to discover whether the blood pressure during anæsthesia was appreciably lower than that observed under basal conditions. (It was not much lower.) One such patient, when first seen, had a casual pressure of 220 and a basal pressure of 153. On the next day, however, his casual pressure was 264 and the basal pressure was 223. Between the first and second observations this patient had learnt from others in the ward that it was probably our intention to administer an anæsthetic and he had expressed his unwillingness. The man was then informed that no anæsthetic would be given and no more elaborate investigations would be made than those he had experienced already. On the afternoon of the same day, a further study of the casual and basal pressures was made, and it was found that both of these had returned to the original levels. Two other experiences of this kind have been encountered, where fear of anæsthesia made it impossible to obtain a true basal pressure and where the removal of the known cause led to a considerable fall in both the casual and basal pressure. It would appear not unlikely that some of the blood pressure decrease following surgical treatment of hypertension is due to a lessening of emotional tone when the operation is over.

A further example of the effect of emotion is seen in the examination of recruits for military service. A consecutive series of 20 men whose blood pressures were found elevated at the routine examination for military service were referred for a second examination. On re-examination under quiet conditions and with the measurements taken repeatedly for about three minutes much lower blood pressures were obtained (Fig. 3). It is of interest that the apex beat was outside the mid-clavicular line in five instances and in two of these the blood pressures at the second examination were below 145 systolic and under 70 diastolic. Evans and Loughlan (1939), in a comprehensive paper on the drug treatment of hyperpiesia, indicate clearly the manner in which blood pressure changes of emotional origin have led in the past to unsatisfactory evaluations of the effects of drugs.

In clinical practice "essential" hypertension refers to elevation of the casual blood pressure. As an average, about half of the elevation above normal of the casual blood pressure, in essential hypertension, represents an increase that depends upon the response of the patient

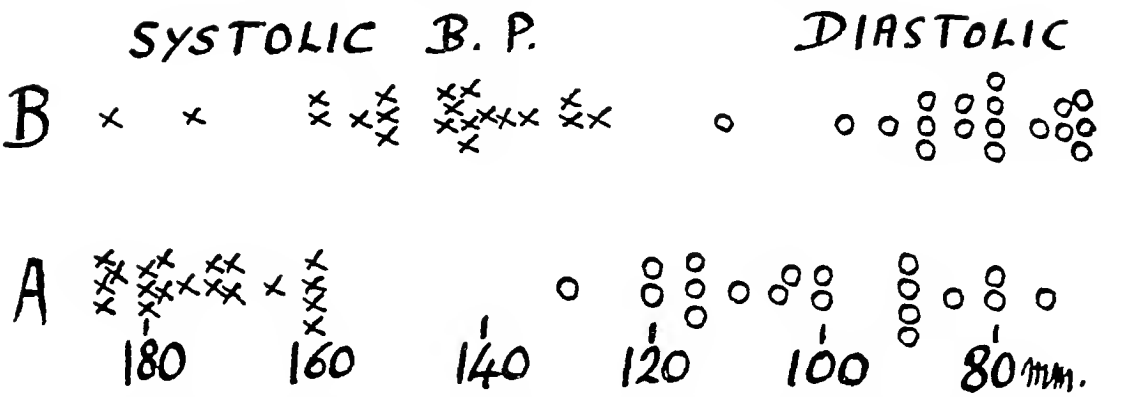

FIG. 3.—Systolic and diastolic blood pressure of recruits with high pressure taken under two different conditions (New Zealand nationals). (A) Systolic and diastolic blood pressures as measured during routine examination of 20 hypertensive recruits. (B) Systolic and diastolic blood pressures of the same men at a re-examination under quiet conditions where 2 or 3 minutes were allowed for the blood pressure to settle.

to mental, emotional, and physical activity in that as an average the blood pressure falls half the way towards normal when the influence of such factors is removed in a relatively short time, by sleep or by a process of physical rest combined with deliberate emotional desensitization. The part played by such factors in determining the degree of elevation of the casual above the basal blood pressure varies in different patients, so that the level of the casual blood pressure does not provide an estimate of the probable basal pressure.

The lability of the blood pressure in a case of essential hypertension may be judged by the degree of difference between the casual and basal pressures. In Fig. 4 it is seen that the patients with the more labile blood pressures are in general those with higher casual blood pressures, but their basal blood pressures are no higher than those of essential hypertension

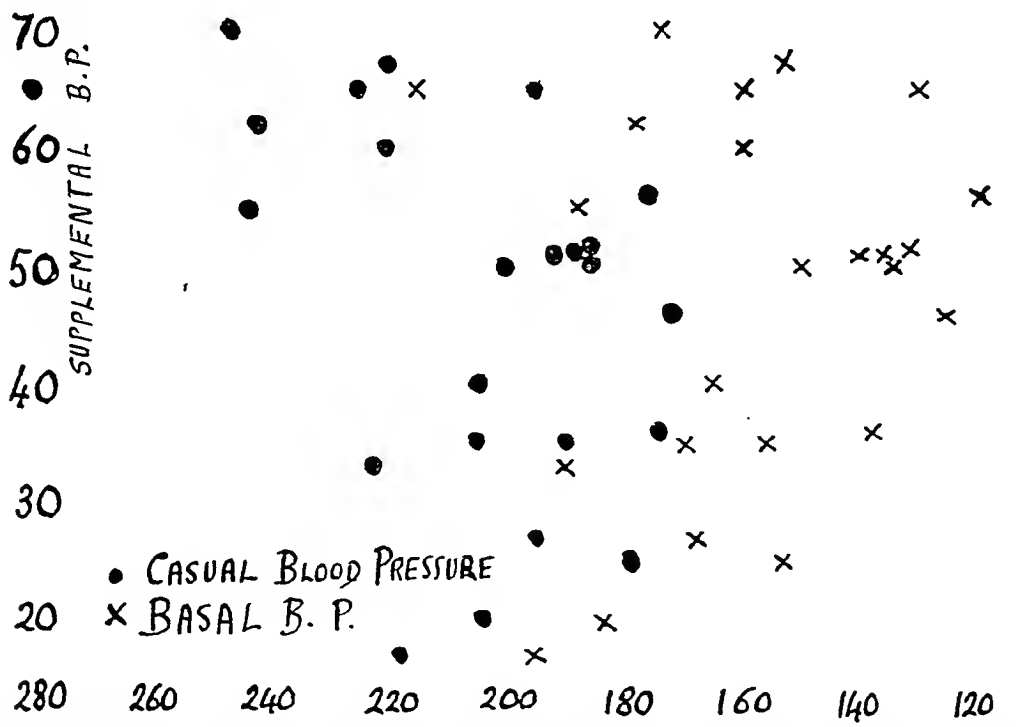

FIG. 4.—Relationship between supplemental (casual minus basal) pressure and the heights of the casual and basal systolic blood pressures. The distribution of points suggests that a rise in the supplemental pressure tends to be associated with a rise in the casual blood pressure but not so much in the basal blood pressure.

patients with less labile pressures.* Thus, if we compare subjects where the differences between the casual and basal blood pressures are between 50 and 70 mm. of mercury with those where the difference lies between 20 and 40, we find that the average of the basal blood pressures does not differ in the two groups whereas the casual pressure is much higher in the 50 to 70 mm. group than in the 10 to 20 mm. group. Hence it would appear that the basal blood pressure is not much influenced by the lability of the blood pressure. It has been shown already (Alam and Smirk, 1938) that the level of the *resting* blood pressure in health shows no correlation with the sensitivity of the subject to blood pressure raising reflexes. Probably the relative importance of the amount of emotional activity and the degree of increased susceptibility to blood pressure raising reflexes, in determining the level of the casual blood pressure, varies from case to case.

It seems desirable to regard the casual blood pressure as made up of two parts, namely, the relatively stable basal blood pressure and a variable " supplemental " pressure. The supplemental pressure is that part of the casual blood pressure which is elevated as the result of the patient's physical, mental, and emotional activity, chiefly the latter, the elevation of the basal blood pressure requires some other explanation.

Summary

In essential hypertension considerable differences exist between the casual blood pressure (i.e. as ordinarily measured) and the basal blood pressure. In a group of 27 patients with essential hypertension, the average casual blood pressure was 195/116 and the average basal pressure was 151/95.

The extent to which the relatively variable casual blood pressure rises above the basal pressure may be termed the supplemental pressure.

The supplemental pressure is that part of the casual blood pressure that represents the response of the cardiovascular system to physical, mental, and emotional stimuli. With rest and habituation to the presence of the observer and his sphygmomanometer, or with sleep, the supplemental pressure falls to, or nearly to, zero.

In Egyptian patients with essential hypertension, both the basal and supplemental pressures are elevated. As an average one-half of the elevation of the casual blood pressure in these cases of essential hypertension is due to elevation of the supplemental pressure which is of a removable nature and due to the effect upon a susceptible individual of his physical, mental, and emotional environment.

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* The suggestion that the height of the casual blood pressure depends mainly on the supplemental pressure, and that the basal blood pressure remained relatively stable did not appear to me to be borne out by Fig. 4. It seemed rather that as the casual pressure increased both the supplemental and the basal pressures increased in proportion. This seems to be confirmed by analysis of the figures. If all the cases are arranged in five groups according to the height of the casual systolic pressure the results are as follows:

casual	*basal*	*supplemental*	*percentage*
246	183	63	25
220	170	50	23
202	165	37	19
195	150	45	23
179	136	43	24

There is a steady decrease in the basal pressure and somewhat similar decrease in the supplemental pressure, the latter forming a fairly steady percentage of the casual pressure in each of the five groups, the figures being 25, 23, 19, 23, and 24 per cent.—Editor.

CASUAL AND BASAL BLOOD PRESSURES
III.—IN RENAL HYPERTENSION

BY

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Received June 1, 1943

In a previous communication it was shown by Alam and Smirk (1938) that the response of the blood pressure to reflexes that raise the pressure was appreciably smaller in renal hypertension than in essential hypertension and even smaller than in health. It is stated by Müller (1921) that during sleep the blood pressure falls much more in essential hypertension than in health or in renal hypertension. It becomes of interest, therefore, to ascertain the relationship between the casual and basal blood pressures in renal hypertension.

Results and Discussion

Our observations were made on chronic cases with a clear history of glomerulo-nephritis, and with a blood pressure of 160 systolic or more. The majority of the patients were Egyptian,

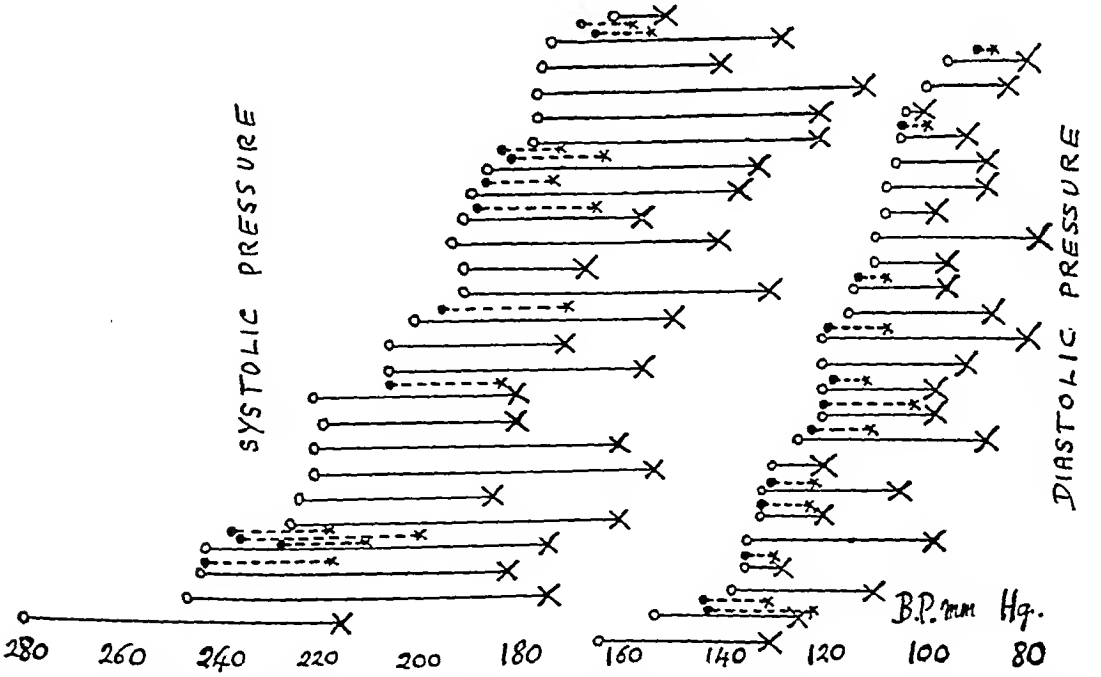

FIG. 1.—Casual and basal blood pressure in renal and essential hypertension. Each horizontal line represents a determination of these pressures, the length of the line indicating the difference between the casual and basal pressure (i.e. the supplemental pressure). The systolic pressures are on the left, the diastolic on the right. Continuous lines represent essential hypertension and dotted lines renal hypertension.

○=casual pressure in an essential hypertension case. ×=basal pressure in an essential hypertension case.
●=casual pressure in a renal hypertension case. ×=basal pressure in a renal hypertension case.

The results are arranged with the higher casual pressures below and the lower above.

and in this the results may be compared with casual and basal pressures obtained in healthy Egyptians or in Egyptians suffering from essential hypertension. A number of additional observations, made on New Zealand patients, are included. The casual and basal blood pressures of hypertensive patients are set out in Fig. 1, and it will be observed that, in general, the difference between these two pressures is much less when the hypertension is of renal origin than when it is of the " essential " type. This statement applies to both systolic and diastolic readings. Hence in renal hypertension the pressure elevation affects the basal pressure more than the supplemental pressure (as defined in the previous paper).

The observation may be related to the common clinical experience that the blood pressure in chronic renal hypertension cases is less likely to show wide variation during a stay in hospital than in patients with essential hypertension. It would appear that rest and emotion due to unfamiliarity with, or excitement produced by, blood pressure measurements have less effect upon the blood pressure in renal hypertension than in essential hypertension. This observation may be correlated with the decreased susceptibility to reflexes that raise blood pressure, which was demonstrated by Alam and Smirk. It would appear that the blood pressure in renal hypertension is no more reactive to vasomotor stimuli than is the normal blood pressure and is less reactive than the blood pressure in essential hypertension.

Summary

The difference between the casual and basal blood pressure is less in renal hypertension than in essential hypertension.

The pressure elevation affects the basal blood pressure more than the supplemental pressure.

It is likely that the blood vessels in renal hypertension are less reactive to vasomotor impulses than they are in essential hypertension.

We are grateful to Professor Soliman Azmy Pacha for his kindness in extending to us the facilities of his post-graduate department.

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LATENT HEART BLOCK

BY

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I have used the term "Latent Heart Block" to indicate a prolonged P–R interval without any manifest degree of block, such as dropped beats or 2 :1 block.

This paper is a clinical study of a series of such cases, mainly from the point of view of the ætiology and significance of the condition. One might guess that latent heart block would be found in the same cases as, but at an earlier stage than, higher grades of heart block; and that a patient would progress from latent to dropped beats, next to 2 : 1, and finally to complete heart block. But such a regular sequence is not common.

Shortly, one can say that latent heart block is found in any type of heart disease at any age without much tendency to progress, and that there is a complete contrast with the well-recognized ætiology of complete heart block, which is atherosclerosis and high blood pressure in elderly patients. As might perhaps be expected, latent block is more often transient than is the case with complete block, but it is often persistent at a fairly steady level for long periods. It is also seen—sometimes to an unusual degree—in hearts that appear to be normal otherwise; here it may be an extreme instance of vagal activity (Fig. 1).

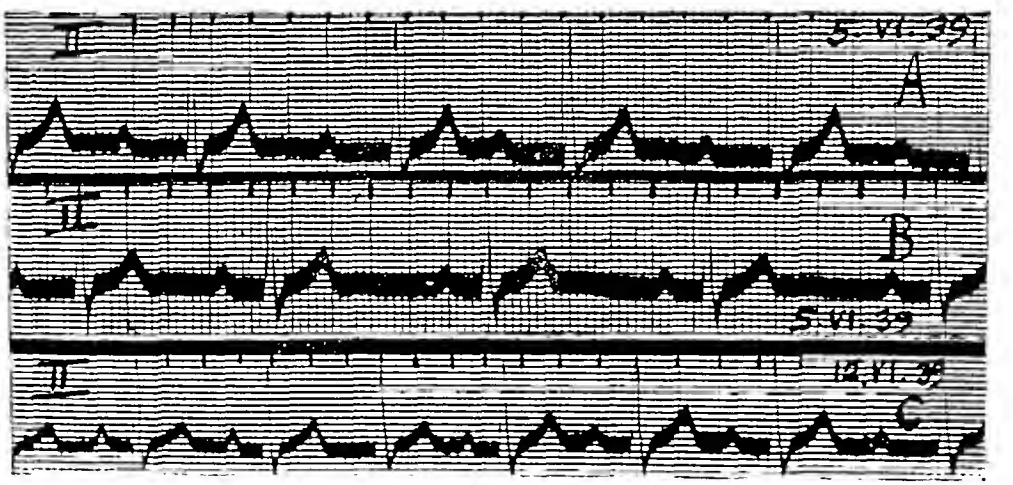

FIG. 1.—An unusual case of latent heart block, with longer and shorter P–R intervals without intermediate grades. From a young man without evidence of organic heart disease. Case 47.
(A) Longer P–R interval of 0·36 sec.
(B) Shorter P–R interval of 0·24 sec., except for the first response.
(C) Shorter P–R interval except for the last response and one instance of ventricular escape.
Of many plates available some showed a long or short P–R interval throughout all three leads, showed a change between the leads and some (mainly chosen for illustration) showed a change recorded while one lead was being taken.
In this and subsequent plates the time marker indicates fifths of a second, and generally inked in at the top.

This lowest degree of heart block, when there is a prolonged conduction time without dropped beats or any higher degree of block, is, as a rule, only recognizable by graphic methods. Cowan and Ritchie (1922) said that it was not often observed and never caused any symptoms, although the patients in whom it occurred usually had obvious symptoms and signs of heart disease. Lewis (1920) mentioned two signs which might lead to its being suspected—a third sound in diastole owing to the auricular systole being separated from the ordinary ventricular sound, and in cases of mitral stenosis the murmur and thrill being isolated and concentrated at a special moment in diastole. These signs are not common, but the custom of taking more electrocardiograms has shown that the condition itself is common. It has therefore seemed worth investigating, and the term " latent " has been chosen as a convenient one for this variety of heart block. It is a true subdivision of heart block, although as a rule it is only made manifest by instrumental methods. The term incipient, which I suggested originally, seems less suitable because it might suggest that this early stage generally progresses sooner or later to a higher grade of heart block, and this is far from being true of most cases.

Any P–R interval of more than 0·20 sec. has been taken as prolonged, or more strictly one of 0·205 or above, as each has been recorded to the nearest hundredth of a second. Many cases with P–R intervals between 0·19 and 0·20 sec. have a conduction time that is prolonged and pathological for them, but unless cardiograms have been taken before there is no way of distinguishing the normal and abnormal at this level, and it is more practicable and more useful to accept the usual upper limit of 0·20 sec.

Chamberlain and Hay (1939) found the average P–R interval (0·16) 0·17–0·19 sec. in different age groups, but recorded a few normal cases where it was 0·22 sec. Hoskin and Jonescu (1940) in young women found most cases between 0·12–0·18 sec., but a very small proportion between 0·18–0·21 sec., the upper limit of normal originally given by Lewis and Gilder (1912).

The papers just quoted show that a few cases with a P–R of 0·21 or 0·22 sec. are normal, and the present investigation confirms their view; but the omission of all below 0·22 sec. would leave out so many pathological cases.

Paul White *et al.* (1941) have recently emphasized the differences often found in measuring the P–R interval in the different standard leads, that in lead II being generally the longest. This will be admitted by anyone measuring many cardiograms, and it would probably be best to work on a standard taken from lead III, as they suggest. But these cases were seen before realizing the extent of this difference or reading his paper, and generally where there were differences an average figure had been taken. In any case, it would have little effect on the very considerable prolongation found in most of these patients, as only 4 per cent of their series showed a variation up to 0·02 sec.

The present series of cases was obtained by looking through 10,000 consecutive electrocardiograms taken at Guy's Hospital in the twelve years 1927–38 (172 cases) and adding all others (61 cases) I had remembered to index from those seen at the Heart Hospital and in private: the latter would fail to include many with only a slight increase in the conduction time, but few of much interest where it was longer; the former would provide an unselected consecutive series, as when there seemed any doubt the P–R interval was measured.

Ten cases with congenital complete heart block have been omitted as they form a special type that has been reported and discussed elsewhere (Campbell and Suzman, 1934a).

This means that about 2 per cent of all patients sent to a cardiac department show latent heart block and rather more than 1 per cent show some clinical degree of heart block.

The 141 cases with latent heart block only have been divided into three grades; (IV A) 31 cases with a P–R interval of 0·26 sec. and above, (IV B) 45 cases with a P–R interval of

from 0·23 to 0·25 sec., and (IV C) 65 cases with a P–R interval above 0·20 but not more than 0·22 sec.

TABLE I

NUMBER OF PATIENTS WITH LATENT AND HIGHER GRADES OF HEART BLOCK

	Guy's Hospital	Heart hospital and private	Total
Number of electrocardiograms	10,000	—	—
Total number of patients	5,320	—	—
Number with some degree of heart block	172	61	233
I. Complete and/or 2 : 1 block without latent	25	11	36
II. Latent and complete or 2 : 1 heart block	15	12	27
III. Latent heart block and dropped beats	17	12	29
IV. Latent heart block only	115	26*	141
A. P–R, 0·26 sec. and above	*23*	*8*	*31*
B. P–R, 0·23 to 0·25 sec.	*34*	*11*	*45*
C. P–R, 0·20 to 0·22 sec.	*58*	*7*	*65*

* This figure is relatively low because they were not searched for systematically, as were the Guy's cases.

ÆTIOLOGY OF CASES WITH HEART BLOCK

The ætiology of cases with latent heart block is summarized in Table II, and for comparison a series of cases, (I) with complete and/or 2 : 1 heart block *without* latent block, (II) with complete and/or 2 : 1 heart block *and* latent block, and (III) with dropped beats but no higher degree of block, have been analysed and tabulated in the same way. It was found that these three grades and the three grades of latent heart block (IV A, IV B, and IV C) could, as far as ætiology is concerned, be combined into three larger groups.

Those with a P–R interval from 0·20 to 0·22 sec. and those with a P–R from 0·23 to 0·25 sec. were combined because they showed no apparent difference, except that (as might be expected) there were among the former more cases with normal hearts and rather more with thyrotoxic hearts. On the other hand, those with a P–R interval from 0·26 sec. upwards showed a much higher proportion of cases with rheumatic fever and acute infections and a much smaller proportion with thyrotoxic or normal hearts. This was also the case with the patients who showed dropped beats, so these were combined into a second group.

Finally there was little ætiological difference between those with 2 : 1 and/or complete heart block, whether they had or had not also latent block, so these were also combined into a third group.

The figures for these three larger groups are expressed as percentages in Table II, after combining some of the smaller ætiological subdivisions to make comparison as easy as possible. The differences are most striking. In the first group with the least prolonged P–R intervals, up to 0·25 sec., 24 per cent had thyrotoxicosis or no apparent heart disease, both these factors becoming much less significant in the second group and absent in the third group with 2 : 1 or complete heart block. Chronic rheumatic heart disease was also of importance in the first group, being the ætiological factor in 22 per cent; this figure falling to 12 per cent in the second, and to 3 per cent in the third group.

In the second group, with the longer P–R intervals of 0·26 and above or with dropped beats, 41 per cent had active rheumatic fever or other acute infections, while this factor was responsible for only 11 per cent of the first group and for only 2 per cent of the third. No other ætiological factor showed a significantly larger figure in this group than in the first group with a shorter P–R interval.

In the third group with 2 : 1 or complete heart block, there was an even more striking contrast: 69 per cent of the cases, against 29 and 23 per cent in the first and second groups, had myocardial disease as the ætiological factor. Syphilitic heart disease was also much more

prominent in this group, being found in 9 per cent against the insignificant figure of 2 per cent in the two former groups. Primary myocardial disease with syphilitic and hyperpietic heart disease were together responsible for 95 per cent of the cases with 2 : 1 or complete heart block, while in the two former groups these three factors combined were not responsible for more than 43 and 40 per cent. Hyperpietic heart disease alone had a much more regular incidence in the three groups, varying only from 12 to 17 per cent. Further subdivision of the myocardial cases did not reveal any striking differences.

TABLE II

ÆTIOLOGY OF DIFFERENT GRADES OF HEART BLOCK (PERCENTAGES)

	IV B and IV C P–R, 0·20 to 0·25 sec.	IVA and III P–R, above 0·26 or with dropped beats	II and I Complete and 2 : 1 heart block with or without latent block
Tonsillitis and acute rheumatism	11	41	2
Chronic rheumatism	22	12	3
Syphilitic	2	2	9
Hyperpietic	12	15	17
Myocardial	29	23	69
Thyrotoxic	13	2	0
No apparent disease	11	5	0
Total numbers	110	60	63

ÆTIOLOGY OF CASES WITH LATENT HEART BLOCK

There were 110 cases with a P–R interval from 0·20 to 0·25 sec.; few of these call for individual comment except that the presumed normals will be enumerated. Otherwise, the diseases from which they suffered seemed to be much the same as might be expected in any other collection of hospital cases.

Of the 110, 48 belonged to the myocardial group (about equal numbers having raised blood pressure or disease of the coronary arteries or heart failure or a large heart without any of these causes being obvious), 36 to the rheumatic group, 14 to the thyrotoxic group, and 12 to the normal group.

There were 31 cases, where the P–R interval was 0·26 sec. or more. Acute rheumatism or tonsillitis or treatment with digitalis were more often responsible for the longer intervals, and in some cases these were the only cause of the P–R interval being prolonged, but in others there was already some degree of prolongation that was increased by a transient infection or by treatment with digitalis. These greatly prolonged P–R intervals will be considered in more detail later (see p. 175). First, however, certain general points about the ætiological groups will be discussed.

Acute rheumatism. Little need be said about this as the prolonged conduction time of acute rheumatism is well known. Parkinson, Gunson, and Gosse (1920) found some degree of block in 30 per cent of their cases during the acute stage. Cohen and Swift (1924) found it over 0·21 sec. in 22 per cent of their cases and somewhat prolonged in 84 per cent, if any increase of more than 0·02 sec. above the normal for that patient was counted as pathological. In a recent study, Keith (1938) found this small increase in 80 per cent of his cases with clinical evidence of rheumatic carditis; he did not say how many were over 0·20 sec., but as the average figure was up to 0·18, a good many must have been so. He brings forward good evidence that the increase is due to vagal activity and, though his title of " over-stimulation of the vagus nerve " might suggest some central factor which would hardly fit in with the general clinical picture, he suggests that the part involved is the vagal nerve terminations in the heart.

All are agreed about the relative rarity of manifest block in these rheumatic cases: Carey Coombs (1924) had only come across six cases where dropped beats were produced by acute rheumatism.

Examples have already been described (Campbell, 1943) and are pertinent in this connection also, as soon after the dropped beats they had latent block alone. In fact, my own records show few instances of classical rheumatic fever as a cause of latent block only and it was more often recorded after a minor relapse, but this is because cardiograms of patients with rheumatic fever were not taken as a routine at Guy's Hospital, but only when there was some special reason.

The return of the P–R interval to normal may be very quick and complete, even after a severe attack. A boy, aged 18, was admitted with a classical attack and had an irregular heart with dropped beats, generally after P–R intervals of 0·25 and 0·37 sec.; after a week it had fallen to 0·18 sec. (Case 13). Here there was little correspondence between the sedimentation rate and the increase of conduction time, for after six weeks, when the sedimentation rate had only dropped from 98 to 47, the P–R interval was down to 0·16 sec. In a man with a very severe attack, the P–R interval was increased from 0·16 to 0·34 sec. (with some dropped beats that were not graphically recorded); three days later it was 0·25 and a week after this 0·19, and after another week 0·17 sec. (Case 22). In a younger man with an attack of average severity it fell from 0·32 to 0·19 sec. in 18 days (Case 54). These three patients all made good recoveries as regards their heart, and a quick recovery in the conduction time is certainly one favourable sign for a good outlook as regards the heart.

Sometimes the P–R interval is increased considerably from what appear to be very minor relapses. In a young man with mitral and aortic disease, it rose during convalescence from 0·20 to 0·26 sec. with a very minor return of pain and was still 0·24 a month later (Case 31). A girl was convalescent after an attack of chorea and slight carditis, and her sedimentation rate had fallen to 6: her P–R interval increased from 0·21 to 0·28 sec. with no other evidence of a relapse except a rise of heart rate from 80 to 90 (Case 52).

In two severe cases the increase of conduction time was no more than in these minor ones. In a boy of 17 with mitral and aortic disease, where it had been about 0·21 for many years, it rose to 0·28 and, finally, to 0·31 sec. (with associated S–T inversion in leads II and III) in his terminal attack of rheumatic fever (Case 36). In a girl with rheumatic aortic regurgitation, where the P–R interval was generally about 0·21, it did not rise above 0·25 sec. in a recurrent attack with pericarditis that was severe enough to produce fairly deep S–T inversion (Case 85).

It is obvious even from this small number of cases that the increased conduction time is not an accurate measure of the severity of the attack or even of the cardiac involvement. Nevertheless, the quick fall towards or to normal is a favourable sign, and often the changes in heart rate, the sedimentation rate, and the conduction time do seem roughly paralell, so that any one is in that case a good measure of the severity of the attack.

Other acute infections are dealt with later.

Chronic rheumatic heart disease. Quite apart from the temporary effect of acute carditis there may be permanent lengthening of the P–R interval as a result of old rheumatic infection.

Typical examples, all of whom had mitral stenosis, were a woman with a P–R interval between 0·23 and 0·26 sec. during four years; a girl of 8 with a P–R interval of 0·23 sec. for three years; a woman of 55 with a P–R interval of 0·23 sec., who was known to have had this for eight years; a woman of 33 with a P–R interval of 0·23 sec., a large P II, and cyanosis of unusual degree (like Case 45), who died a few months later ; and a man of 29 with a P–R interval of 0·24 sec., who had paroxysmal auricular tachycardia at a rate of 146 without any change in the P–R interval.

As a rule the lengthening was not extreme, but there was one striking exception—a girl with mitral stenosis who was under regular observation for eight years with a P–R interval that increased gradually from 0·26 to 0·36 sec.; apart from tachycardia there was no evidence of any return of active carditis, unless a silent carditis precipitated failure in the last two years of her life (Case 45; see Appendix).

In many of the cases with a long P–R interval due to active rheumatism some slight prolongation had been noticed even before the infection.

There were six patients, who had latent heart block when first seen and later developed auricular fibrillation. One girl with rheumatic aortic incompetence, whose P–R interval had been raised from its normal 0·21 to 0·31 sec. by unwise digitalization during recurrent subacute rheumatism, developed fibrillation four years later. At least three of the others had mitral stenosis; a girl, who had rheumatic fever when 4, had a P–R interval of 0·21 when 10, and fibrillation when 15; a young woman who had a P–R interval of 0·22 sec. during the fifth month of her pregnancy, developed fibrillation after her confinement; and a woman of 37 who had gradually been forced to restrict her very active life, was seen with bronchitis, a P–R interval of 0·24 sec., and a very large P II, and five months later developed fibrillation. No recurrence of active rheumatism was suspected in these last two, but it is, of course, one exciting cause of the onset of fibrillation in some cases.

In addition, two cases first seen with fibrillation had long P–R intervals when normal rhythm was restored with quinidine; in one of these, normal rhythm continued for some years and the P–R

interval was 0·24 sec., so no question of active infection arose. In one man with flutter a long P–R had been enough to produce a heart rate of 72 owing to 4 : 1 block (Case 41, see Appendix), but another in whom the P–R interval was 0·24 sec. had had fairly rapid flutter simulating fibrillation before it was stopped.

In such a mixed group of patients, it is not easy to know the prognosis, and at the time I had not regarded latent heart block as a specially unfavourable sign, perhaps because in those who had done badly there were often other unfavourable signs. Looking through the cases as a whole, it seemed to me they had done less well than might have been expected. The finding of a long P–R interval of 0·24 or above should, therefore, lead to a very careful review of the patient's life and activity and these should be limited until further observation allows gradual progress. No doubt it is partly because latent heart block and large P waves are often found in hearts that are badly damaged in other ways, but it may be that sometimes latent block is a sign of a rheumatic infection that is otherwise silent, and this possibility should be carefully considered.

Myocardial and hyperpietic disease. There seems little special to say about these cases. It was not regarded as a finding of special interest or significance, so no great effort was made to follow them up, but it was often noted that a P–R interval of 0·21–0·24 sec. remained stationary for one or two years. Coronary atheroma (with coronary thrombosis or simple angina), hyperpiesis, congestive heart failure—alone or in combination—or an enlarged heart without evidence of these other factors were all common.

Rarely did any patient, found by chance to have latent heart block, develop complete block. But there were several instances where a patient, sent up because Stokes-Adams attacks or heart block were already suspected had, when examined, latent block only, and later was seen again when he had a higher degree of block. Such cases with 2 : 1 or complete block will be dealt with in a subsequent paper and the relationship of these to latent block will then be discussed more fully. One old man included in this series was sent up with a history of Stokes-Adams attacks and was found to have latent block only (*Case 58*; see Appendix), but probably if he had been seen more often, complete heart block would have been recorded as he died two years later in another Stokes-Adams attack. In all other instances (unless *Case 59* is another exception) such patients were seen at other times with higher grades of block and will therefore be dealt with in the later paper.

Case 55 (Appendix) was of interest, both because of his P–R of 0·35 sec. and because he had anginal pain in a phantom arm.

Case 44 (Appendix) would have been included in the group with no heart disease and the change attributed to his obesity, if he had not been followed up; ten years later the blood pressure was 180/120, but it is possible that this was a coincidence as the P–R interval, though still long, was shorter (Fig. 2).

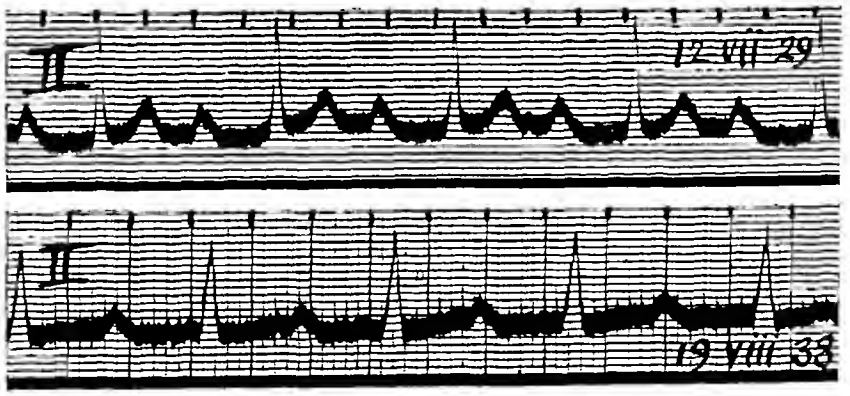

FIG. 2.—Latent heart block with obesity from a man, aged 40, in 1929. Case 44.
(A) 1929, P–R of 0·36 sec. with blood pressure 130/80.
(B) 1938, P–R of 0·31 sec. with blood pressure 180/120.

Bundle branch block. The association of this with latent block was much more common than would be expected if it were a chance coincidence. Apart from the patients with higher grades of block and B.B.Bl., there were 5 of the 141 with latent block who had B.B.Bl. also (2 of the 31 with a P–R interval of 0·26 sec. or above).

This led to my looking through 25 consecutive cases of bundle branch block, excluding any that were already in this series. Sometimes it was not easy to measure P–R, because it was difficult to know where QRS began, and this led to even greater differences than usual between the measurements in the different leads. Using lead II, where it often seemed the longest, the average P–R interval was 0·17 sec.: in 7 it was from 0·12 to 0·15 sec.; in 11 it was from 0·16 to 0·19; in 6 it was 0·20 sec. or a little more; and in 1 only was it as long as 0·24 sec.

Thyrotoxicosis. Nearly one tenth of all the cases with latent block had thyrotoxicosis, but a very large number of thyrotoxic patients were sent for cardiograms. In my own cases where cardiograms had been taken from time to time over a longer period, the P–R interval was not often lengthened without an added infection, so the high proportion may have been due to the large amounts of Lugol's iodine, which many of these patients were taking before operation. This was not the whole explanation, for sometimes it was seen when the patient was not having iodine, and in one case the P–R interval was 0·22 sec. when she was admitted for her first operation and 0·14 sec. six months later, when she was improved but not yet well and was having a second operation: on both occasions she was having Lugol's iodine.

Myxœdema. There were also three cases with latent heart block and myxœdema. In one the P–R interval was 0·23 sec. when there were low-voltage or flat T waves and only 0·20 when the T waves were upright after thyroid treatment. In another the P–R interval was 0·23 without thyroid, and 0·21 six years later when she had again been without thyroid for several weeks. I was surprised at these findings as some years ago in reporting the cardiographic changes in eight cases of myxœdema (Campbell and Suzman, 1934b) comment had been made on the low voltage P that increased with thyroid treatment, but not on the P–R interval. In five of the eight cases there was no significant change. However, three of the eight showed a P–R becoming shorter by about 0·03 sec. after thyroid treatment—0·24 to 0·20 sec., 0·21 to 0·18 sec., and 0·19 to 0·16 sec.—so that this should be added as one of the fairly common features of the myxœdema heart.

Congenital heart disease. Among the cases with latent block there were three examples of this. A girl, aged 13, with coarctation of the aorta and a patent ductus arteriosus, had a P–R interval of 0·26 sec.; she died a year later. A man, aged 28, with bicuspid aortic valves, great enlargement of the heart, and congestive failure had a P–R interval of 0·24 sec.; he died six months later. A woman, aged 35, with moderate enlargement of the heart and an auricular septal defect had a P–R interval of 0·23 sec.; she was alive three years later but was troubled with hæmoptysis.

It seems likely that in all these the latent block was a subsequent development and not part of the original congenital condition, for they were all sick people.

Trauma. There was no cases in this series where latent block seemed to be due to trauma, but such have been reported. One has been added recently by Barber (1942) where a P–R interval of 0·35 sec. persisted for at least five months. Dr. J. R. B. Hern has shown me an example of long P–R, 0·24 sec., following blast from a bomb: though she had orthopnœa and œdema of the legs, the main damage was at first thought to be pulmonary and this was supported by the X-ray findings and the continued cough; however, a year later the P–R interval was still 0·24 sec.

Diphtheria. No cases have been included as diphtheritic. One woman, aged 42, may be mentioned as a possible instance; seen because of extrasystoles, she had a P–R interval of 0·26 sec. and some cardiac enlargement, and a history of diphtheria as a child (*Case 34*). One girl with a severe relapse of thyrotoxicosis had a P–R interval of 0·22 sec. from the third to the eighth month after diphtheria, but its duration before her attack was not known. A past history of diphtheria has been mentioned in some others (Cases 47, 49, and 55), but in none was there evidence that the prolongation dated from that attack, and it may have represented no more than the expected incidence of past diphtheria in any community.

Bruce Perry (1939) has mentioned two cases of complete heart block persisting for several years after diptheria, but this is certainly rare. Jones and White (1928) investigated 100 patients who had suffered from diphtheria at least five years before; in 70 the attacks had been severe. In no case could they find any evidence that any chronic heart disease had been produced, and on electrocardiographic examination there was nothing more than one example of nodal premature beats with ventricular escape.

Other acute infections. Tonsillitis seemed the most important infection after acute rheumatism. Sometimes it was difficult to be sure that an apparent attack of tonsillitis was not really rheumatic, as illustrated by the following example.

Case 43. A boy of 15, with a doubtful history of growing pains when he was 4, was seen a few days after a sore throat that had followed a 100-mile cycle ride. He was pale and thin, with red tonsils, but no signs in his heart except a P–R interval of 0·26 sec. After his admission to hospital, the sore throat recurred with very little rise of temperature, but he was found to have several rheumatic nodules, and later had one attack of paroxysmal tachycardia. During the month in hospital the P–R interval fell to 0·21 sec.

In spite of this difficulty I feel satisfied that in many cases there were no grounds for suspecting a rheumatic infection. Two have already been quoted where dropped beats and afterwards latent block followed tonsillitis that did not appear to be rheumatic (Cases 5 and 17). The latter has been under observation for 10 years without any evidence to suggest rheumatism, although her P–R interval rose to 0·32 sec. after a transient sore throat, quickly returning to 0·16, at which level it has remained for 10 years. The two patients that follow are further examples without any evidence of rheumatism.

Case 56. A healthy-looking boy, aged 14, came to hospital ten days after an attack of tonsillitis that had lasted three days. He had no history of rheumatism and no symptoms except occasional faintness during the past two years. Nothing was found on examination except a P–R interval of 0·27 sec. and two weeks later this had fallen to 0·21 sec.

Case 59. A boy, aged 18, who had a Stokes-Adams attack three weeks after tonsillitis and came to hospital four days later with a P–R interval of 0·28 (Fig. 3), that quickly fell to 0·16, is reported in the appendix. There was nothing to suggest that the illness was really diphtheria.

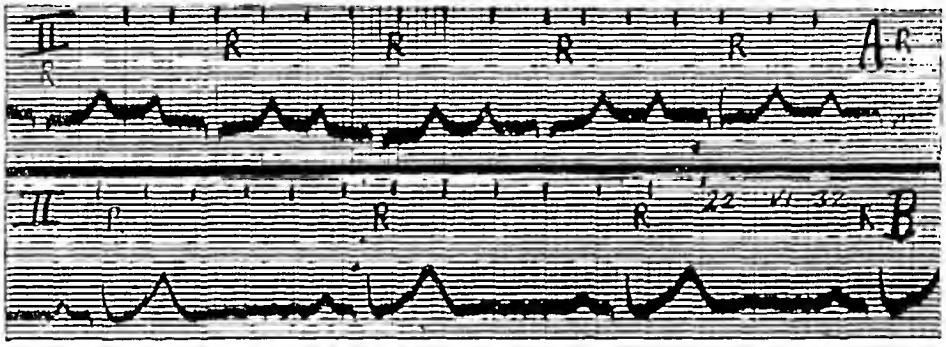

FIG. 3.—Temporary latent heart block after tonsillitis from a young man whose heart was otherwise normal. Case 59.

(A) Lengthened P–R interval, 0·28 sec., three weeks after an attack of tonsillitis and four days after a Stokes-Adams attack.

(B) Rapid return of the P–R interval to normal, 0·16 to 0·17 sec This curve was taken five weeks after (A), but the P–R interval was 0·18 sec. a week after, and 0·16 to 0·17 two weeks after (A).

Two other patients were included in this group as one was in hospital with a sore throat and the other came up soon after one (Cases 42 and 47; see Appendix). But there was not the same speedy fall of the P–R interval, and follow-up study after 1 and 5 years respectively showed that they still had equally long P–R intervals. This and some other unusual features suggest that the latent heart block may really have preceded their tonsillitis and that they ought to be included as cases without any evidence of heart disease. If so, the range of possible variation in the P–R interval under vagal influence must be considerably widened.

CASES WITH NO APPARENT HEART DISEASE

9 of the 65 cases with a P–R interval between 0·20 and 0·22 sec. were regarded as having no heart disease, though in each case some question had been raised that led to their examination. They were as follows: a girl of 17 with habit spasm and a girl of 19 with obesity; the remainder were men, three being under 40 (31, 28, 27) with pleurisy, an anxiety state, and sinus bradycardia with sinus arrhythmia; three being between 40 and 50 (42, 48, 49) with extrasystoles, vaso-vagal attacks, and a duodenal ulcer; and the ninth, a man of 67 with gallstones. It is possible, of course, that some minor degree of heart disease escaped detection in these cases, but it seems more likely that a P–R interval of 0·21 or even 0·22 sec., though unusual, is not outside the limits of normal.

Case 94. A man, aged 27, who was only seen because of the slow and irregular heart found when he was up for life insurance, was of interest because he was probably an instance of the effect of vagal activity. His heart rate varied between 35 and 48 and his P–R interval was 0·22 sec.

There were 3 of the 45 patients with a P–R interval of from 0·23 to 0·25 sec., who were thought to have normal hearts, and these must be considered in a little more detail.

Case 84. A girl of 21, with a diagnosis of hysterical fits, was sent for examination of her heart because she had twice had chorea, the last time four years before. The P–R interval of 0·24 sec. may have been the result of her attacks of chorea, but nothing abnormal was found about her heart.

Case 72. A man, aged 39, had been under observation for some years with duodenal ulcer and had done well. On one occasion at out-patients, he complained of dyspnœa, and though nothing else was found, his P–R interval was 0·25 sec. On later occasions it had reverted to 0·20 sec., so probably this was due to some transient infection in a heart that was otherwise normal. If so, he should of course be placed in the group with acute infections, but in the absence of more definite evidence it seemed best to discuss him here.

Case 77. A man, aged 50, had fairly severe bronchial asthma of long standing. His heart was thought to be normal but the P–R interval varied between 0·23 and 0·25 sec. It is possible that this may have been the one early sign of heart disease that was not detected otherwise.

In none of these three cases was there any other sign of heart disease.

The main difference between these two groups is that in those with a P–R interval of from 0·20 to 0·22 sec. there was little or no reason for suspecting the heart, while in the group of possible normals with a P–R interval of between 0·23 and 0·25 sec. there was, in every case, some suspicion of early heart disease, though the latent block was the only certain evidence.

One would not expect to find any patients with normal hearts with a P–R interval of 0·26 sec. or more, but three must be mentioned as other evidence of heart disease was trivial or absent.

Case 51. A man, aged 41, was thought to have a normal heart, though at first there was some doubt if the dyspnœa of which he complained might possibly be post-influenzal. In 1931 his P–R interval was 0·24 sec. In 1934 I got him to resume work, and in 1939 his symptoms were much the same and certainly no worse; the P–R interval was 0·27 sec. and records taken most years suggested that this really had been a gradual but irregular increase. His heart was not enlarged and there was no other evidence of disease.

It is of interest because it is possible that it represents a slight progressive change that in the course of several more years will result in a higher grade of heart block recognizable clinically. But this course is unlikely for many of these cases have been followed for years, and such changes have been looked for and yet we have no other similar example.

Case 40. Here, the interpretation is difficult. In 1927, when 43, he was thought to have a P–R interval of 0·35 sec. (Fig. 4). He complained of extrasystoles, paroxysmal tachycadria, and symptoms that were due to anxiety. He was seen at intervals during the next ten years, and never had any symptoms suggesting heart disease, nor a P–R interval longer than 0·16 sec. He was not taking any drug known to affect the heart at the time the long interval was observed.

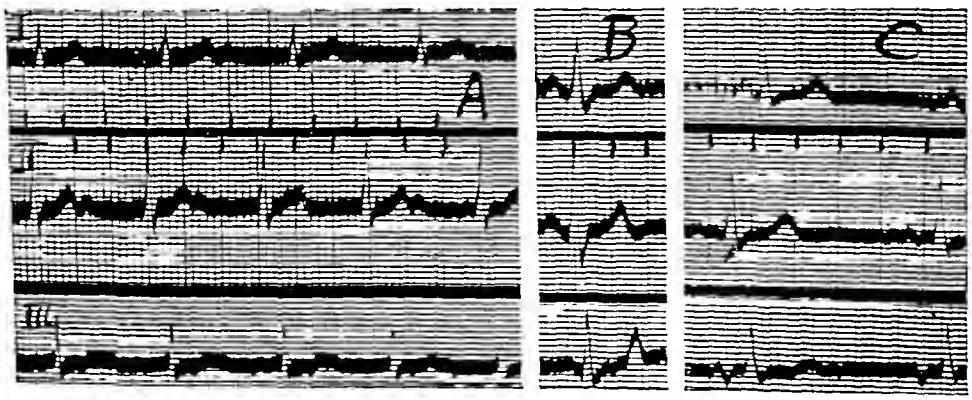

FIG. 4.—Temporary latent heart block of high grade. Case 40.
(A) Cardiogram of 1927, with a P–R interval of 0·35 sec. No other explanation seems possible, especially in view of the fourth response in lead II being premature, but still with the same P–R interval.
(B) A week later, and (C) ten years later, both these showing a normal P–R intervals of 0·16 sec.

It is possible that this was an unusual result of a minor transient infection; although an extreme example it would not be much more extreme than some others.

Case 49. A man, aged 28, was sent for a cardiogram because of extrasystoles. The diagnosis of tuberculosis of the lungs was considered but not proved, for though he complained of cough and loss of weight, the X-ray was inconclusive. His heart was thought to be normal except for the extrasystoles, which sometimes after exercise were so frequent as to simulate paroxysmal auricular fibrillation, and a variable P–R interval which changed from 0·20 to as long as 0·36 sec. There was no gradual increase, but on two occasions where records were obtained (and as far as could be judged on several other occasions) there was suddenly a very long P–R interval up to 0·36 sec. with the P-P interval remaining constant, and the R-R interval lengthening appreciably (Fig. 5). Such a

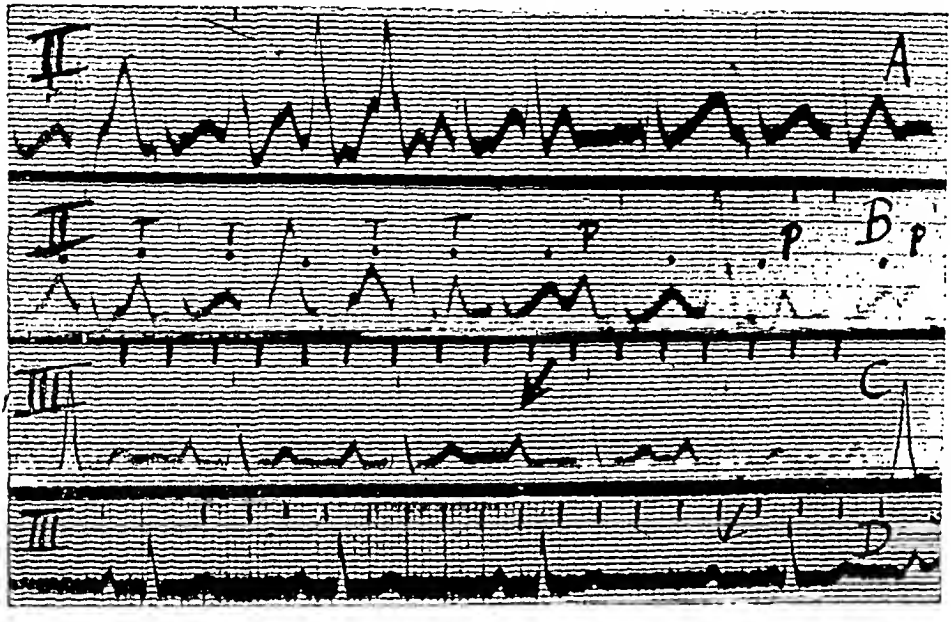

FIG. 5.—Irregular latent heart block of high grade. Case 49.

(A) and (B) Irregular rhythm after exercise.
(C) April 1935 and (D) June 1935, showing single P–R intervals of 0·36 sec., interrupting P–R intervals of 0·20 sec. These are probably vagal effects in a normal heart.

sudden change must almost certainly be a vagal effect and related to sinus arrhythmia, but it is curious that even so it should not occur more gradually. Nor was there any sinus bradycardia such as has been described in Case 94 with much less lengthening of the P–R interval. After eight years he was written for and seen again. He had been getting on well and had been working regularly, with no symptoms. His heart rate was 80 with much irregularity after exercise; this seemed to be (*a*) an extreme sinus arrhythmia, the rate doubling, but not suddenly as with S-A block, and at times; (*b*) a gross irregularity that was not influenced by respiration and lasted for some beats only. X-ray confirmed that there was no enlargement of the heart and showed some old calcified areas below the right clavicle.

Cases 42 and 47 in the appendix should be noted in this connection; at the time the latent block was thought to be the result of attacks of tonsillitis, but its persistence and some other features suggest that in these two as well as in *Case 49* it may really have been an unusual vagal effect.

THE LENGTH OF THE P–R INTERVAL

As would be expected, P–R intervals a little above the normal are very much more common than those greatly above it. There were a large but diminishing number at each hundredth of a second from 0·21 to 0·24, a moderate but more slowly diminishing number at from 0·25 to 0·28, and a smaller and fairly steady number (at each hundredth of a second) from 0·29 to 0·37 sec. Those with P–R intervals of 0·21 and 0·22 and those with P–R intervals of 0·23 and 0·24 have been combined, and so on, partly because the numbers were small and partly because there was a little tendency to record the measurements by even numbers. The full figures are shown in the second column of Table III.

TABLE III

LENGTH OF THE P–R INTERVAL

Length of P–R interval in seconds	Number of cases			
	(IV) Latent heart block only	(III) Dropped beats and, at other times, latent block	(II) Complete or 2 : 1 block and, at other times, latent block	Total
Less than 0·20 sec.	—	2	5	7
0·21 0·22	65	4	5	74
0·23 0·24	39	1	6	46
0·25 0·26	13	3	3	19
0·27 0·28	8	6	1	15
0·29 0·30	2	3	2	7
0·31 0·32	4	4	1	9
0·33 0·34	3	2	2	7
0·35 0·36	4	1	0	5
0·37 0·38	2	0	0	2
0·39 0·40	1	1	0	2
0·44	—	0	1	1
0·47	—	1	—	1
0·56	—	1	—	1
Total number	141	29	26	196
Average P–R interval ..	0·24 sec.	0·28 sec.	0·25 sec.	

A smoothed curve has been drawn in Fig. 6. It falls very sharply at first between 0·24 and 0·25, but then levels out and shows little further tendency to fall after 0·29 until it practically comes to an end at 0·40 sec., above which there were only single cases.

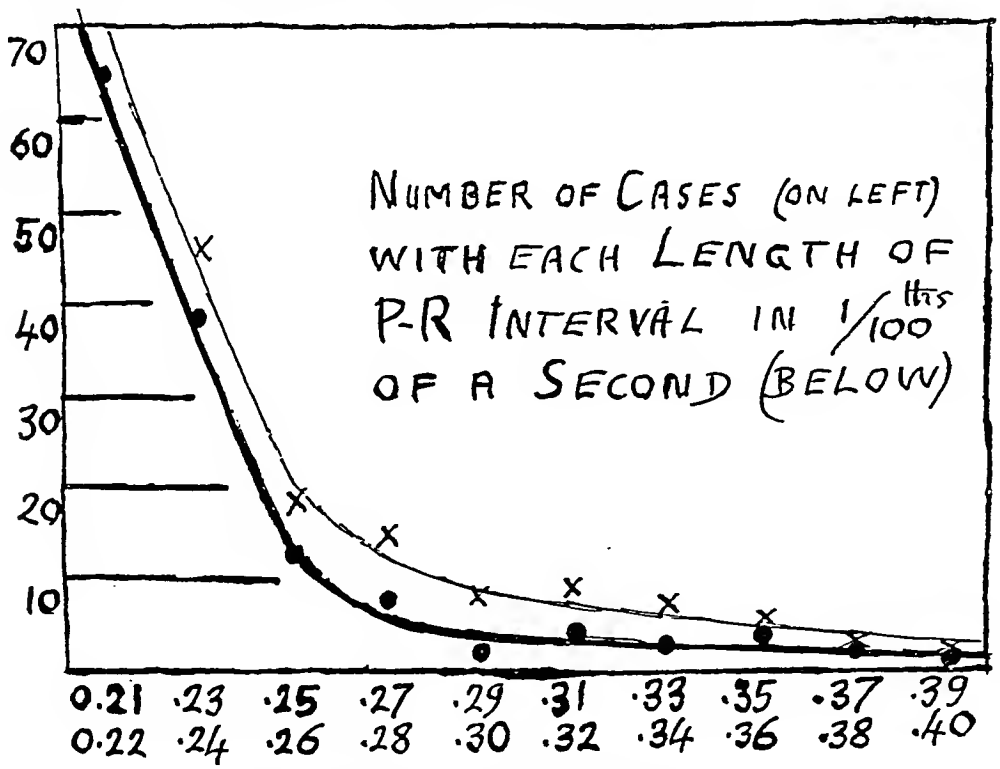

FIG. 6.—Number of cases with latent heart block.

Abscissæ, length of the P–R interval in hundredths of a second; ordinates, number of cases.
The thick line below includes the 141 cases with latent heart block only.
The lighter line above includes the additional 53 cases that had dropped beats or higher grades of heart block at one time and latent block only.

M

There were 141 cases with heart block that was latent only; 29 others had sometimes dropped beats and sometimes latent block; and another 26 had sometimes 2 : 1 and/or complete heart block and sometimes latent block. One might expect in each of these groups also, either that the frequency distribution would be similar or possibly that the length of the P–R interval would vary round a much higher average figure.

This was not so; in those with latent heart block only, 74 per cent of the cases had a P–R interval of 0·24 sec. or less (46 per cent, 0·21 or 0·22); in those with dropped beats, only 24 per cent had a P–R interval of 0·24 or less, and 65 per cent had figures of 0·27 sec. or above; those with 2 : 1 and/or complete heart block also, was more like the former than the latter, 61 per cent having a P–R interval of 0·24 or less, but being more equally distributed through this range.

In those with latent block, the average P–R interval was 0·24 sec. and most of the cases were between 0·21 and 0·24 sec. In those with dropped beats, the average was much higher, 0·28, and most of the cases (55 per cent) were between 0·27 and 0·34 sec. In those who had at times higher grades of heart block the average was intermediate and nearer to that of latent block, viz. 0·25, with a range more equally distributed between 0·19 and 0·26 sec.

The full figures have been given in Table III. Table IV shows certain statistical data which may make the results clearer to some. The median is the point above and below which there are equal numbers of cases; the mode is the point at which the largest number of cases are grouped: if the distribution curve was symmetrical these two figures would of course be the same as the average, but with such a skew distribution curve for latent heart block there is much divergence; in the other two groups the divergence is much less.

TABLE IV

AVERAGE AND MEDIAN P–R INTERVALS IN DIFFERENT GRADES OF HEART BLOCK

	P–R intervals (in seconds) in latent heart block		
	(IV) Latent block only	(III) With, at other times, dropped beats	(II) With, at other times, 2 : 1 or complete block
Average	0·239	0·278	0·254
Median	0·226	0·283	0·240
Mode	0·21	0·28	0·24
Quantiles	0·210–0·244	0·246–0·322	0·215–0·270
Usual range	0·21–0·24	0·27–0·32	0·19–0·26

The quantiles give the points between which half the cases lie; one-quarter being outside and above, and one-quarter outside and below. The usual range was chosen by inspection (before the quantiles were known) and has no exact mathematical meaning. It has been thought worth giving these additional figures because with such a wide range of variation average figures alone give a very imperfect picture.

CASES WITH THE LONGEST P–R INTERVALS

The ætiology of latent heart block in general has been discussed; in this section those with the longer P–R intervals will be considered in more detail.

Of the 31 cases where it was 0·26 sec. or above, 11 had rheumatic heart disease. They were on the whole young but not very young patients, at an age still liable to acute rheumatism rather than at the age most prone to suffer from the late results of old rheumatic heart disease. Only one was over 27 and the average age was just under 24 years. In 4 of the 11 the lengthening was transient and certainly due to an acute infection; in 3 it was transient and probably due to an acute infection (though in both these groups there was often a slightly

prolonged P–R interval before and/or after the transient increase); and in 4 it was persistent and not due to any active infection.

There were 12 of the 31 with myocardial disease, generally coronary atheroma or high blood pressure. They were, as might be expected, older patients, the average age being 58 and only three being under 50 years of age. The only two in whom the heart disease was not gross and obvious were *Case 34* (see p. 169) and *Case 44* who had developed high blood pressure after 10 years, but might have been described as normal as nothing was found at fault except his obesity and latent block (see p. 168).

One case had congenital heart disease (*Case 37*, see p. 169).

This left 7 cases where the heart was thought to be free from any organic disease. They were mostly young adults with an average age of 26 years. In 3 of the 7 no cause was found (*Cases 40, 49, and 51*; see p. 171). In the other 4 the long P–R interval were thought to be due to an attack of tonsillitis without any evidence that this was rheumatic. In 2 of these 4 the lengthened P–R disappeared quickly, confirming this view (*Cases 56 and 59*, see p. 170); but in 2, a recent follow-up has shown that it has persisted for 1 and 5 years respectively, and other features, the extreme sinus arrhythmia and the P–R interval of either about 0·36 or about 0·24 sec. suggest that possibly the attacks of tonsillitis were not the cause and that these were unusually marked effects of vagal activity (*Cases 42 and 47*, see p. 179).

This gives a very different picture, clinically and ætiologically, from that found with the higher grades of heart block. This is confirmed even by the most cursory glance at Table V. Here the 15 cases with a P–R interval of 0·30 sec. or more are shown : 9 were between

TABLE V

CLINICAL NOTES OF CASES WITH A P–R INTERVAL ABOVE 0·30 SEC.

Case No.	Sex and Age when first seen	Years under observation	P–R interval		Diagnosis of heart condition	Remarks
			longest	shortest		
45	f. 15	7	0·40	0·26	Rh. mitral stenosis	Lengthened by digitalis, but finally 0·36 without it.
49	m. 28	8	0·37	0·20	Normal	Extrasystoles and tuberculosis.
58	m. 77	3	0·37	—	B.P. 280/100	Stokes-Adams attacks ; died after 3 years.
44	m. 40	9	0·36	0·31	Obesity	1919: obesity, B.P. 130/80; 1938: B.P. 180/120.
47	m. 20	1	0·36	0·24	Normal	Recent sore throat; ? incidental.
40	m. 43	10	0·35	0·16	Normal	Long P–R once only.
55	m. 52	1	0·35	0·35	Myocardial	Coronary atheroma; ? recent infarction.
57	m. 54	—	0·34	0·26	Rh. mitral stenosis	Congestive failure: increased by digitalis.
35	f. 24	1	0·34	0·14	Rh. aortic incompetence	? Rheumatic carditis but no other evidence.
42	f. 21	6	0·33	0·28	Normal	Recent sore throat when first detected.
50	f. 25	2	0·32	0·25	Rh. mitral st.	Recurrent carditis.
54	m. 24	—	0·32	0·19	Rh. mitral st.	During rheumatic fever.
48	f. 18	5	0·31	0·20	Rh. aortic incompetence	Mainly due to digitalis, but also recurrent rheumatism.
36	m. 14	6	0·31	0·21	Rh. mitral and aortic	Lengthened during terminal attack of rheumatic fever.
41	m. 68	2	0·30	0·25	Myocardial	Flutter with 4 : 1 block; digitalis restored N.R.

14 and 25 years of age; 7 had rheumatic valvular disease; 4 (or 5 if Case 44 be included) were thought to have hearts that were free from organic disease, though 2 gave a history of sore throats; and only 3 were elderly men with signs of cardiac disease, such as are generally found with complete heart block.

There were also 12 cases, described in the paper as partial heart block with dropped beats (Campbell, 1943; most are listed in Table II on p. 56) who had at other times latent block only, with a P–R interval of 0·30 sec. or more. As a group they resemble the cases just described very closely: 8 were between 18 and 30 years of age; 5 had rheumatic heart disease; 5 were thought to be free from organic heart disease, but acute infections seemed a rather more important factor here; and only 2 were elderly patients (and in one of these the block was due to digitalis). In both these groups efforts have been made to keep in touch with most of the patients for many years, and only one has gone on to complete heart block (Case 58). Often the long latent block fell to a less prolonged figure (say, 0·21 to 0·25), but sometimes it persisted.

The patients with the highest grades of latent block are therefore a rather special group. In some, acute infections are the cause and the block is temporary; in others, the reason is obscure, and in some of these there seems little else the matter with the heart.

Summary and Conclusion

Latent heart block is a convenient term for a conduction time that is prolonged without any dropped beats or higher degree of block.

All those where the P–R interval was above 0·20 sec. have been included in this series. About 2 per cent of the patients sent to a cardiographic department showed this change, and 141 cases were analysed. The incidence fell very rapidly from 0·21 to between 0·24 and 0·25 sec., and then more slowly to 0·29, after which it was steadier, cases being seen at all levels up to 0·40 sec.; longer P–R intervals than this were very rare. In nearly half (46 per cent), the P–R interval was not more than 0·22 sec. In nearly one-quarter (22 per cent), it was 0·26 sec. or more.

In addition, 29 cases, which sometimes had dropped beats and sometimes latent block only, and another 27, which sometimes had 2 : 1 and/or complete heart block and sometimes latent block only, were analysed.

When there was latent block only, the P–R interval was most commonly between 0·21 and 0·24 sec. When latent block interrupted complete and/or 2 : 1 block the figure was much the same with a rather wider common range, 0·19 to 0·26 sec. On the other hand, when there were at times dropped beats, and at other times latent block only, the P–R interval was on the average longer, and was generally from 0·26–0·32 sec., possibly because more of these cases were due to a transient acute infection.

As a rule, latent block did not progress to higher grades of heart block. In many it diminished as the effect of an acute infection disappeared; in some it remained at a fairly constant level; and in some it was found, occasionally or from time to time interrupting complete and/or 2 : 1 heart block.

The ætiology varied somewhat in the different groups. Where the P–R interval was from 0·20 to 0·25 sec., all types of heart disease were represented in much the same proportions as might be found in any collection of cardiac cases.

Where the P–R interval was 0·26 or above, the ætiology was more like that found in cases with dropped beats: 41 per cent (as against 11 per cent with a P–R interval from 0·20 to 0·25 sec.) had acute rheumatism or other active infections, mostly tonsillitis, and there were fewer cases with thyrotoxic or normal hearts.

Cases with latent block and at other times 2 : 1 or complete block were ætiologically like the cases with complete heart block, i.e. older patients with atheroslcerosis or primary myocardial disease (69 per cent against 26 per cent in the two previous groups, or 86 per cent against 39 per cent if hyperpietic cases were included).

Acute rheumatic carditis was a common cause of P–R intervals that were much prolonged, to 0·26 sec. or above. Chronic rheumatic heart disease occasionally caused these longer

values, but was more often responsible for the slighter increases from 0·20 to 0·24 sec. Other acute infections sometimes produced quite a long P–R for a time; these including attacks of tonsillitis that were almost certainly not rheumatic.

Latent heart block, especially of the lesser grades, was seen in all types of chronic myocardial disease. Even here it seemed rare for it to progress gradually to complete heart block, though often it interrupted complete or 2 : 1 block, sometimes after surprisingly long intervals.

Both in thyrotoxicosis and myxœdema, long P–R intervals were observed, and the relationship of this to iodine therapy in thyrotoxicosis needs more investigation.

No instances of latent block due to trauma were included in the series, though such cases have been reported; and one due to blast has been mentioned.

There were no cases where latent block could with certainty be attributed to diphtheria, but such a history was noted in some cases as a possible cause that could not be excluded.

Some curious cases have been described in which P–R intervals, even up to 0·30 sec. or more, were found without any other evidence of heart disease. As some of these persisted they did not seem to be due to infection, and it is suggested that exceptionally overaction of the vagus may produce unusually long P–R intervals. In some, which have been described rather fully, the longest P–R intervals were irregular or intermittent.

Some few cases with a P–R interval up to 0·22 sec. or even higher seemed to be normal in every way.

Appendix of Case Notes

Cases with Acute Rheumatism

Some typical cases have been referred to in the text (p. 167) and in a previous paper (Campbell, 1943, p. 56). A less usual case is added below.

Case 35. C., aged 24, complained that she had fainted after a hot bath; probably her doctor would not have sent her to hospital had he not found a murmur. She had free aortic regurgitation with some enlargement of the heart, and though there was no rheumatic history slight mitral stenosis confirmed that it was rheumatic. Her attack seemed like an ordinary faint and had none of the characteristics of a Stokes-Adams attack so that a P–R interval of 0·34 sec. was a surprise. We expected this would prove to be a permanent feature of her heart, but she was told to lead an easy life and return in two weeks in case a change should show there had been active carditis.

She resumed her normal life and was not seen again till she was written for after six months. She had no symptoms except the slight degree of dyspnœa to which she was accustomed. Her P–R interval was now 0·14 sec. This gives an important indication of the changes that may be going on in the heart unsuspected, and means that even in the young an attack of faintness may occasionally indicate cardiac damage.

Cases with Chronic Rheumatic Heart Disease

Several of these have been quoted shortly in the text, and the following is given in more detail because of the unusual length of the P–R interval.

Case 45. I. J. had chorea and rheumatism at 11, and four years later (1932) was found to have enlargement of the heart (13 cm./22 cm.) and high-grade mitral stenosis. She complained of cough and dyspnœa and was unusually cyanosed. The P–R interval was prolonged, and on 12 occasions during the next year it varied between 0·24 and 0·28 sec. Her heart rate was generally 108–120, but there was no other evidence of recurrent rheumatism.

During the next two years, treatment with digitalis improved her condition as regards her dyspnœa and cyanosis, but the heart rate remained about 96–108. It lengthened the P–R interval to between 0·32 and 0·40 sec. Although she was seen nearly every fortnight during three years no dropped beat was ever observed (Campbell, 1942, p. 140).

In 1934 she started work and was seen less regularly. In 1936 some œdema of the feet developed and she began having short paroxysms of tachycardia, lasting up to half an hour. She was never quite so well after this, but continued at easy work with short periods in hospital for another two years. The P–R interval varied between 0·32–0·36 sec. and was often this length when she was not taking digitalis. She was lost sight of after December 1937, and died elsewhere in February 1939 and we have not been able to get details of her final illness.

Here a P–R interval of 0·28–0·36 sec. persisted for at least 7 years, and even when she was taking digitalis no dropped beats were ever observed.

Cases with Myocardial Disease

Case 41. *Latent block, producing spontaneous* 4 : 1 *block when there was auricular flutter.*

A man, aged 68, with a large heart and a blood pressure of 160/100 came to hospital, complaining of cough and dyspnœa. His pulse rate was 76, but this was found to be due to auricular flutter with spontaneous 4 : 1 block, which after exercise changed to irregular 2 : 1 block. He was given Nativelle's digitaline, and when he came to hospital a fortnight later said he had taken 1/600 grain t.i.d. the first week, and q.i.d. the second week. This had restored normal rhythm and the P–R interval was 0·30 sec., compared with his normal of 0·24, which was found during the months following when he was not taking digitalis. In this case the latent heart block was as helpful as digitalis treatment would have been in producing such a degree of block that the ventricular rate was normal as long as he was not exerting himself.

This is not uncommon with auricular fibrillation where some natural degree of block in an elderly patient helps in the same way that digitalis would by reducing the ventricular rate; but with fibrillation it cannot be demonstrated so elegantly as in this case of flutter.

Case 44. *Latent block and obesity, followed after some years by high blood pressure.*

A man, aged 40, was admitted to hospital for fatigue, dyspnœa, and headaches, the latter due to severe myopia in the right eye. All his symptoms were attributed to his excessive weight of 16 stone, and nothing else abnormal was found except a P–R interval of 0·34–0·36 sec. (Fig. 2). The Wassermann reaction was negative. He improved with thyroid and dieting.

Two years later his condition was somewhat better as he had kept his weight lower, but the P–R interval was still 0·36 sec. He had taken no thyroid for some time as it upset him, but had restricted his diet.

After another eight years he was re-admitted for increasing dyspnœa. He had never felt well but he had been at work all the time and had kept his weight to 15 stone by eating very little except bread and butter. The P–R interval was 0·31 sec. and the blood pressure, which had been 130/80 in 1929 and 145/95 in 1931, had risen to 180/120; the first sound was reduplicated. No other abnormality was found, except that the cardiogram now showed flat T waves as well as the latent heart block.

Case 55. *Latent block and angina, with anginal pain felt in a phantom arm.*

One of these patients is of interest, not only because of his long P–R, 0·35, but because he had anginal pain in a phantom arm. His right arm was blown off in France in 1917. Eighteen years later, in May 1935, he began having anginal pain which started across the chest and spread down the right phantom arm with great regularity. In October 1935 his pain became worse and he may have had a cardiac infarct, but there was no cardiographic proof of this. In May 1936, when he was 52, he came to hospital as his angina was troublesome and persistent. Nothing was found on examination except a P–R interval of 0·35 sec. which remained constant for the three months he was under observation. He had had diphtheria in 1933.

We were much interested in the pain he felt in his phantom arm because of its occurrence so long after the loss of his arm, but not surprised as it seemed to us that with a pain that was normally referred from the centre to the arm, it must still be felt there if the arm was able to give rise to sensations of any sort: we did not realize till seeing the paper by Cohen and Wallace Jones (1943) that such a case had not been reported. Dr. S. Suzman made many attempts to study his reaction to nitrites, but it was not easy to provoke the pain by any exercise he took while under observation as the onset was less regular than in most cases of angina.

Case 58. *Stokes-Adams attacks: latent block only while under observation.*

A fine, healthy-looking old seaman, aged 76, had a Stokes-Adams attack. He had no other complaints except a little dyspnœa. A year later, although he had no more attacks, he was sent to hospital and the cardiogram showed a P–R interval of 0·37 sec. He gave a clear account of his pulse getting slower with more dropped beats, and stated that the pulse rate often fell to 33, especially in bed in the morning, so that it is almost certain he had complete or 2 : 1 heart block. His heart was enlarged, his blood pressure 280/100, and the Wassermann reaction positive. He was not seen again and died suddenly three years later.

Cases with Tonsillitis

Case 5 and *Case 17* have been reported already (Campbell, 1943, p. 57) as at one stage they had partial heart block with dropped beats, but are pertinent here as at a later stage they had latent heart block only.

Case 59. S. S., aged 18, had tonsillitis, a first attack, and was at home for a week without seeing his doctor. He returned to work but did not feel as well as usual. After two weeks at work he woke up feeling sick, and on his way to the lavatory fell down unconscious and cut his face severely. His doctor found his pulse rate 34, and kept him in bed till he came to hospital four days later.

Nothing was found abnormal except an altered first sound, slight albuminuria, and a P–R interval of 0·28 sec. (Fig. 3A); a week later this was 0·18, and after another week 0·16 sec. (Fig. 3B). He felt quite well and continued at work. It seems unlikely that this was an undiagnosed attack of diphtheria.

If he had not been seen again this would seem a simple case where the P–R interval was lengthened by tonsillitis and where there had been complete heart block with a Stokes-Adams attack, his recovery being complete and rapid. But nine months later when asked to come to hospital again he had a curious cardiogram. He had been quite well until " influenza " a month before and had had no more attacks of faintness or loss of consciousness. The usual P–R interval was now 0·23 sec., but sometimes it was much shorter as though there was ventricular escape (R_4 in Fig. 7D and to a lesser extent

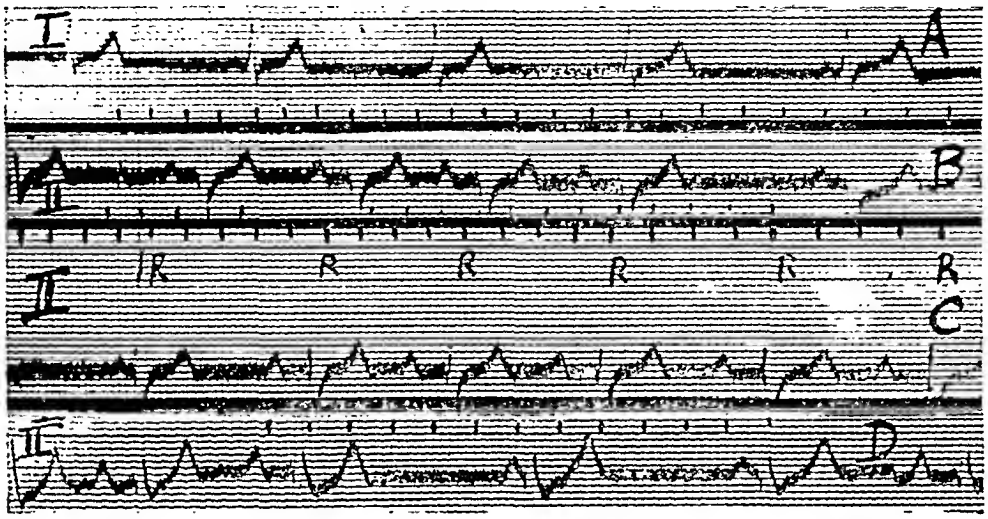

FIG. 7.—Sinus arrhythmia with variation of the P–R interval, which is at times much below its usual length of 0·23 sec., probably due to ventricular escape. From the same Case 59 as Fig. 3, all taken nine months later (17/2/33), shortly after an attack of influenza.

(A) Ventricular escape (see text).
(B) Shorter P–R interval after a pause in the sinus rhythm.
(C) Ventricular escape (R1), nearer to the auricular wave than in (A).
(D) Sinus arrhythmia with ventricular escape twice during the slower period.

R_6 of Fig. 7B). Sometimes this happened where there was a longer pause, probably during the expiratory phase of sinus arrhythmia. Sometimes, however, it happened without any sinus arrhythmia (see Fig. 7A): there the P-P intervals were constant, but the R-R intervals were shorter so that the first four P–R intervals became shorter or non-existent, until the fifth R-R interval being longer allowed P–R to reappear; nodal rhythm arising in different sites could explain this, but the regular P-P rate makes this unlikely, and frequent ventricular escape at a rather rapid rate seems the most likely explanation.

Cases with Tonsillitis that may have been merely incidental, in which event they should be included as Cases with no other evidence of organic heart disease. Cases with no other evidence of heart disease have been described in the text (pp. 170–172).

Case 42. A nurse, aged 21, was admitted with a sore throat, a temperature of 102, and a pulse rate of 80. The third day she felt well and her temperature was normal, but her heart rate was found to be irregular and about 50. Dropped beats were suspected and two days later the P–R interval was 0·29–0·32 sec. (Fig. 8). A week later it was unchanged, and three weeks after when she had been feeling perfectly well, a record was obtained that was at first thought to be dropped beats but was sino-auricular block or perhaps extreme sinus arrhythmia as the long P-P interval was much less than twice the normal: no progressive lengthening of the P–R interval of 0·32 sec. was observed. A week later when she was allowed up, P–R was again 0·30 sec. and regular.

She was not seen again for two months as she was on holiday, feeling quite well. Four months after the sore throat that had lasted only two days, sino-auricular block or extreme sinus arrhythmia with other periods regular was again observed, with the P–R interval unchanged; in the absence of symptoms or other signs she was allowed to resume work.

After another year, during which she had continued at work, she felt well and showed no physical signs, except that P–R was still 0·30 sec. She gave no history of rheumatism at any time. It was at that time thought unlikely that she had any degree of heart block before her short illness.

During the next four years she carried out her work as a nurse without any symptoms or disability,

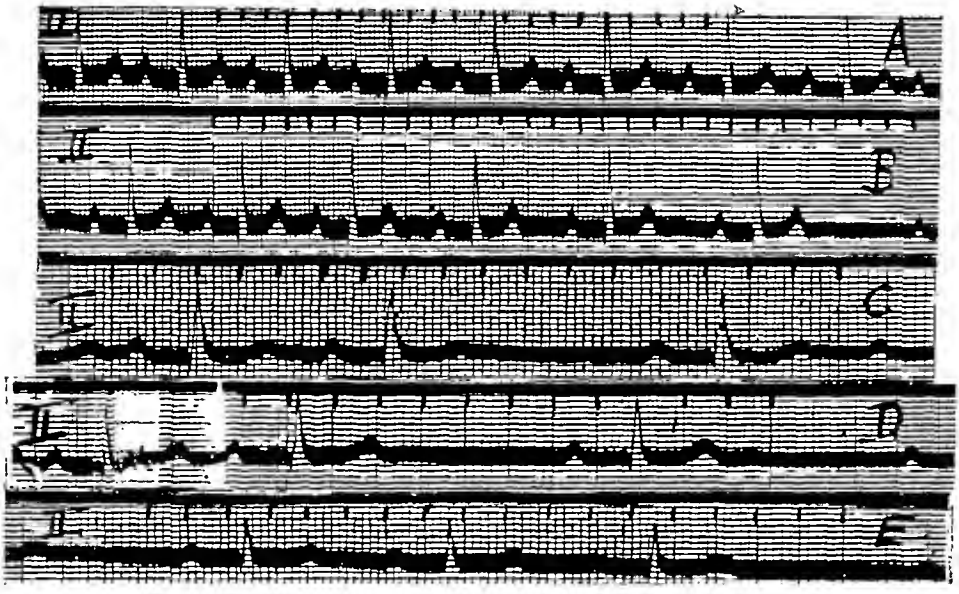

FIG. 8.—Extreme sinus arrhythmia with a long P–R interval, persisting for at least five years. Case 42.
(A) The most usual finding with a rate that is nearly regular (shortest R–R, 0·86; longest R–R, 0·96).
(B) On the same date, changing to a much slower rate—the six P–P's being 0·92, 0·92, 1·02, 1·07, 1·18, and 1·54 sec. (C), (D), and (E) all show marked sinus arrhythmia, the last two being taken during deeper respiration.
(C) Was taken on 14/2/38, three weeks after a sore throat (which may have been incidental); all the others were taken on 2/3/39.
In 1943 the P–R interval was still 0·31; the rate was regular when recorded, though at other times there was some irregularity that did not appear to be associated with respiration.

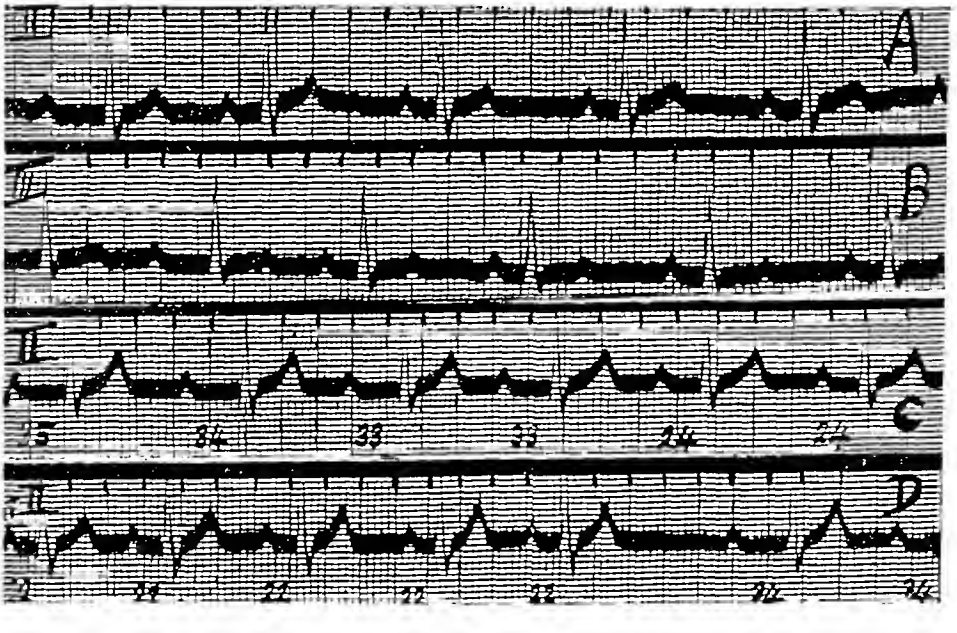

FIG. 9.—Changes of long and shorter P–R intervals. Case 47; see also Fig. 1.
(A) and (B) Both show the change from the long to the shorter P–R interval at the beginning of the picture (5/6/39.)
(C) Shows better the change from the long to the shorter P–R interval; the P–P intervals are nearly constant, but shorten a little from 0·96 to 0·87 sec. (26/6/39.)
(D) Shows the change from the shorter to the long P–R interval; the last P–P interval before the long P–R is much longer than usual (but not twice as long); as a rule, however, the rate of the heart with the long or with the shorter P–R interval was the same. (26/6/39.)

leading a normal life in every way. Nevertheless, her P–R interval was still 0·31 sec. as it had been four years before. Her heart rate was between 56 and 64 with some slight irregularity of the sinus type that was not, however, associated with respiration. There were no abnormal physical signs.

At first she was thought to be a case of partial heart block following tonsillitis as in the two cases described with dropped beats (Cases 5 and 17), one of these also being a nurse; but its long persistence without any other symptoms and the association with sinus arrhythmia that was at times extreme enough to simulate sino-auricular block suggests that it may be a physiological, though unusual finding in a patient with very high vagal tone.

Case 47. A young man, aged 20, came to hospital complaining of breathlessness and pain in the left side of the chest which had been present most days for a year. He was anxious about tuberculosis as he had a bad family history, but clinically and on X-ray examination his chest was normal. He was liable to sore throats and had been ill with this three weeks before for four days, but had not seen his doctor as it seemed no worse than usual. He had fainted once nine months before. He gave no history of rheumatism, but had had diphtheria as a child.

Nothing was found on examination except that his P–R interval was about 0·24 sec. For this reason only he was asked to return the following week, when his P–R interval was sometimes 0·24 and sometimes 0·34 sec. This was observed on many occasions during the next nine months, the longer P–R interval always being between 0·32 and 0·36, and the shorter always between 0·22 and 0·26 sec. On one occasion only he was seen with a heart rate nearly 100 and the interval was as short as 0·20 sec.

Generally the rate was relatively slow, about 60, and sometimes as slow as 44. There was no general difference in the heart rate whether the P–R interval was about 0·24 or about 0·34 sec., the average rate in both cases being 61. On one occasion (see Fig. 9D) there was a change to the long P–R interval after a pause and perhaps with a slower rate afterwards, but on the same day another plate showed the reverse change without any change of rate (see Fig. 9C). Most often, all the beats in one lead showed the same P–R interval, but records showing the change over have been picked out for illustration.

During the year he was under observation there was no regular change in his symptoms, which were sometimes better and sometimes worse. His sedimentation rate was normal; an X-ray of his chest was clear; and the throat surgeon reported that though he had frequent slight attacks of tonsillitis there was no focal sepsis. He was not unduly thin and was putting on weight.

At first the long P–R interval was attributed to his recent tonsillitis, but the relatively slow heart with the variable P–R interval suggest a high degree of vagal tone, and it is possible that this was usual with him and quite independent of the recent attack. Attempts to trace him recently have not been successful.

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AURICULAR FIBRILLATION LATE IN THE COURSE OF DIPHTHERIA

BY

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Auricular fibrillation has been recorded as occurring in diphtheria during two distinct phases of the disease. During the acute phase, when the heart is gravely damaged, it may be incidental to progressive failure, and, much more rarely, it may be a later manifestation without any other sign of myocardial damage. It is an example of this second type that we record here. It may be some measure of the rarity of the association of auricular fibrillation with diphtheria that of three standard American text-books of cardiology, Fishberg (1940), Pardee (1941), and White (1937), only one (Fishberg) mentions it, and that only in a simple statement that in diphtheria the pulse may be irregular as the result of extrasystoles, auricular fibrillation, and other disturbances of rhythm. Burkhardt *et al.* (1938) found no case of auricular fibrillation in 140 adults with diphtheria, examined electrocardiographically every second or third day of their stay in hospital. We cannot accept the statement of Neubauer (1942) that 2 of his 100 cases of diphtheria with heart lesions showed transient auricular fibrillation, because, in the only examples he records (his Fig. 14), the rhythm of one is regular in lead III and the irregularity in lead II could be extrasystolic, and in the other (his Fig. 15), who had a severe heart lesion, it cannot be auricular fibrillation for the ventricular rhythm is in fact regular. Parkinson (1915) recorded the case of a youth, aged 22, who was admitted to an isolation hospital on November 8, 1913, suffering from pharyngeal diphtheria. On November 30, he developed heart block, followed, on December 11, by auricular fibrillation, without any other evidence of myocardial damage. He was discharged from hospital on January 17, 1914, still fibrillating. Seen finally in June, he was still without symptoms and could walk seven miles without dyspnœa, but he was still fibrillating; how much longer it lasted is unknown. It was learnt that he was accepted for Army service in India in 1914, that he remained on active service until 1919, when he came home on leave after having had malaria; he was then in the best of health but six weeks later he developed pneumonia and died. This is the only case record similar to ours that we have found, but, owing to war conditions, we have been unable to make an exhaustive search. The occurrence of fibrillation as an isolated manifestation of myocardial damage in diphtheria is sufficiently rare to justify this case record.

Case Notes

K.S.L., a dentist, aged 39, was serving in the R.A.F.V.R.

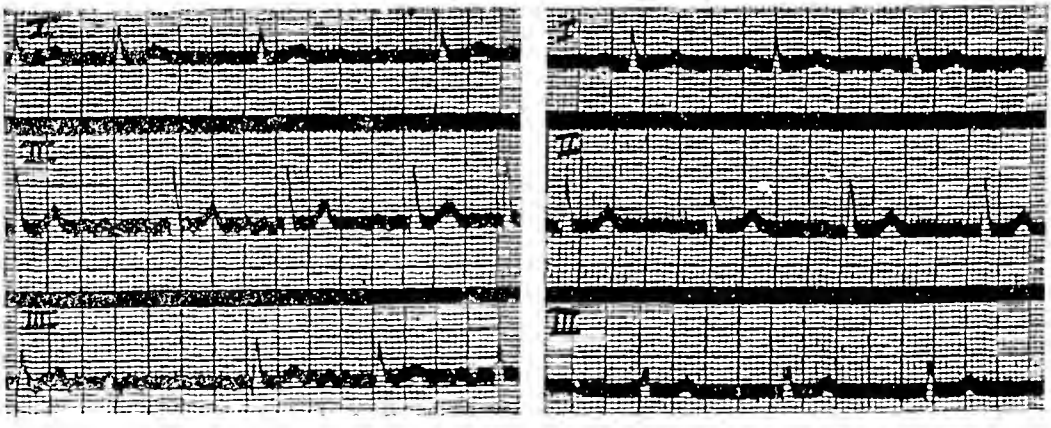
His mother had died of a stroke following hypertension. His father, aged 70, had just recovered from an attack of hypertensive congestive failure. His brother had been confined to bed for two years, following what was stated to be a cardiac complication of measles.

He gave no history of any illness other than complaints of childhood. He had never had rheumatism or chorea. He had always been fit and well; a keen cyclist, he had cycled as much as 140 miles in a day.

On October 6, 1942, he began to feel ill with a sore throat. He did not report sick until two days later, when a diagnosis of follicular tonsillitis was made and he was sent to bed. On October 12, he returned to duty, not feeling unduly ill but rather weak. In retrospect, he remembered seeing, on the first day of his illness, a greyish-white membrane on his throat, which disappeared after one day, leaving a red inflamed area. After a few days he felt much better and cycled 40 miles without undue fatigue.

On October 19 he began to get regurgitation of food through his nose, but, otherwise, felt well and continued at duty. He did not report sick until November 10, when the medical officer realized what was the matter; he was admitted to Torquay Isolation Hospital on the same day. On November 20 he noticed the sudden onset of tachycardia and irregularity of the pulse. It was considered that this was due to extrasystoles and, in view of the likelihood of mycardial damage, he was ordered complete rest. About this time he also noticed tingling of his hands and feet. About December 10 the palatal paresis began to improve and he was allowed to get up gradually. He was discharged to sick leave on December 19. Whilst he was in hospital three throat swabs were taken, but all were negative for *K.L.B.*; no serum was given.

Whilst on sick leave he led a quiet life, walking short distances only. He felt reasonably well but was easily tired by quite mild exertion. Palpitation was conspicuous, occurring both at rest and on exertion, but he was not breathless. He also noticed an unpleasant tingling in his feet when walking about. On resuming duty, on February 23, 1943, he was referred to one of us (C.R.T.L.). The apex beat was displaced about half an inch to the left, and he was fibrillating, but without pulse deficit. The heart sounds were normal and the blood pressure approximately 140/80. There was some hypoalgesia over the soles of the feet and some loss of deep pain sense in the legs. Fibrillation was confirmed (P.C.G.; Fig. 1 A). He was trans-

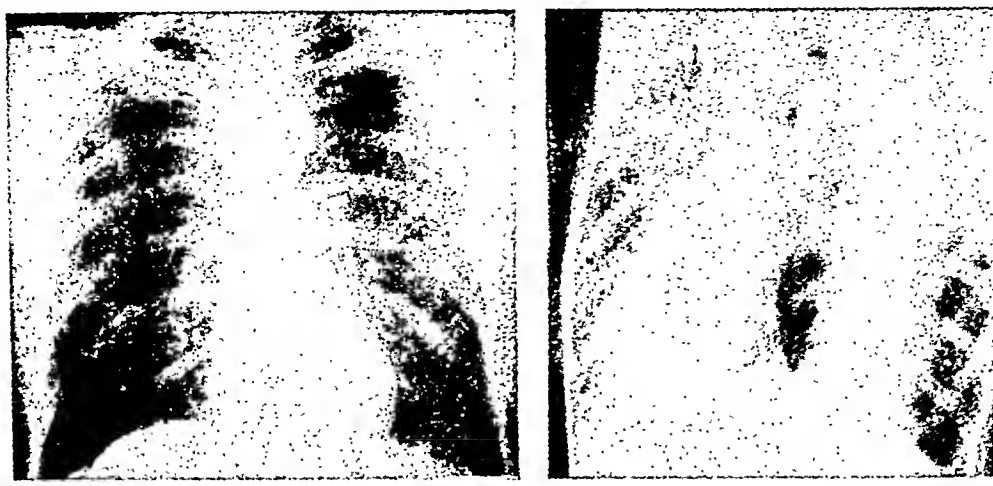


A B

FIG. 1.—(A) Electrocardiogram taken 24/2/43, showing auricular fibrillation. Rate about 80.
(B) Electrocardiogram taken 23/4/43, showing normal rhythm. Rate 68.

ferred to an R.A.F. Hospital, where a radiogram showed no enlargement, but his blood pressure was recorded as approximately 140/100. Quinidine, 5 grains t.i.d., was started on March 5, and after he had had 15 grains the pulse became regular. On April 19 he returned to duty feeling perfectly well. On that day he was seen by A.M.G.C., who found that his nervous system was normal, except for some weakness and displacement of the uvula to the right and diminished vibration sense in both legs. He gave an excellent history and, on being complimented on this, said he had been interested in his illness even to the point of introspection; only now did he refrain from taking his pulse every hour. The second electro-

cardiogram (Fig. 1 B) showed no abnormality except small P waves. The heart rate was 68. The apex beat was in the fifth space, four and a half inches from the mid-sternal line, and was rather forcible. The blood pressure, sitting and recumbent, taken three times in each position, was consistently 145/95. The radial arteries did not seem thickened. The fundi



A B

FIG. 2.—(A) Teleradiogram showing normal size of the heart.
(B) Teleradiogram in right anterior (II) oblique position.

were normal. Later, radiograms (Fig. 2) showed no enlargement of auricles or ventricles The urine was examined and found to be normal, chemically and microscopically.

COMMENTARY

The association of peripheral neuritis with myocardial damage in diphtheria is well known. Burkhardt *et al.* (1938) found the incidence of peripheral nerve palsies very high in those cases of diphtheria that showed electrocardiographic changes. From another angle, Walshe (1941) stated that in polyneuritis there is always some myocardial damage. Our case conforms with these views and supports the suggestion that it is desirable to seek for cardiographic changes in all cases of diphtheria, irrespective of severity, that have peripheral nerve lesions.

There is a possibility, emphasized by Geoffrey Bourne (1940) that some chronic local change in the heart, the commonest probably being vascular disease, may account for incomplete recovery after diphtheritic myocarditis. In our case there was a family history of arteriosclerosis and our patient himself showed some evidence of this, though only if his diastolic pressure is accepted as such.

Another feature of interest is the long period that elapsed after the onset of diphtheria before auricular fibrillation was established. This was also found in Parkinson's patient. In both cases fibrillation occurred during convalescence.

SUMMARY

In a man of 39 years old, we record auricular fibrillation, which arose during his convalescence from diphtheria. It lasted for 112 days, when it was stopped by quinidine. Except for his palpitation, it was unaccompanied by any symptoms referable to the cardiovascular system. It was associated with multiple peripheral neuritis, which preceded its onset by 32 days. There was a family history of arteriosclerosis and some slight evidence of this in the patient himself.

We are indebted to the Medical Director General, R.N., and the Director General of Medical Services, R.A.F., for permission to publish this paper, to Wing Commander A. Nelson-Jones for supplying notes on treatment given at the R.A.F. hospital, and to Surgeon Commander A. R. Thomas, R.N.V.R., for the radiographic investigation, and we particularly wish to thank Dr. John Parkinson for his advice and assistance.

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COMPLETE AURICULO-VENTRICULAR DISSOCIATION WITH HIGH VENTRICULAR RATE IN PAROXYSMAL TACHYCARDIA

BY

CLIFFORD G. PARSONS

Received July 19, 1943

The ventricular rate in auriculo-ventricular dissociation is commonly less than 60, and in 1923 Hewlett was able to find only 14 recorded instances in which this rate was exceeded. Most of these patients were under the influence of digitalis and all but one of the remainder had organic heart disease; the exception was a woman whose dissociation developed after tonsillectomy (White, 1916). In Hewlett's own case the P–R interval was considerably prolonged, and during attacks of dissociation the ventricles usually, although not invariably, beat more rapidly than the auricles; most reported examples which he quotes had auricular rates exceeding the ventricular. His observations led him to conclude that the occurrence of dissociation is favoured, on the one hand by the presence of partial A-V block or by the administration of digitalis, and on the other by factors tending either to decrease the auricular or to increase the ventricular rate. White's patient, for example, having recovered from a spontaneous attack of dissociation, would still develop the abnormal rhythm if the carotid sinuses were stimulated, the auricles slowing until the A-V node escaped. Hewlett felt that the rapid ventricular rate in his own patient, together with the conspicuous effect on the rhythm of changing vagal tone, were evidence that the pacemaker lay in the A-V node.

Cowan (1939) reviewed ten cases of dissociation and of these only two had sound hearts, both having a slow ventricular rhythm; all ten had ventricles beating either at the same rate or rather faster than the auricles. This point is emphasized by Katz (1941) for distinguishing between dissociation, which he regards as a functional condition, and heart block, which is frequently due to organic disturbance. " In dissociation the rate of the ventricles is equal to or faster than that of the auricles, while in A-V block, with rare exceptions, the reverse is true."

Barker and his colleagues (1943), in an interesting paper, discuss the occurrence of A-V block in paroxysmal auricular tachycardia. After reviewing 17 previously reported cases they describe 18 of their own and compare the condition with auricular flutter, pointing out, amongst other features, that carotid sinus pressure slows the ventricles without influencing the auricular rate, and usually fails to arrest the attack. The degree of block encountered ranged from partial block with occasional dropped beats, through 2 : 1 and higher grades of A–V block, to two examples of complete heart block. These last two patients had regular ventricular rates of 84 and 26 respectively; one, a woman aged 26, had organic heart disease, and the other was a man of 70, reported by Singer and Winterberg (1922).

A somewhat different abnormality of rhythm was described by Barker (1924), who reported a case of paroxysmal auricular tachycardia in which an attack was disturbed by a brief phase of ventricular tachycardia. The ventricular contractions were slightly irregular and no auricular complexes could be identified. The patient had had attacks of palpitations for 36 years and her heart was otherwise sound.

The report which follows concerns a patient subject to attacks of paroxysmal auricular tachycardia. She had no evidence of organic heart disease and had had no drugs. A spontaneous, short-lived attack in which auricles and ventricles beat quite independently, each at a rate well in excess of 100, was recorded during her first appearance at hospital.

Case Report and Electrocardiograms

A woman of 29 attended hospital in November 1942, complaining of attacks of palpitation which she had had for 7 years. The paroxysms occurred two or three times a day, always started and ended abruptly, lasted from ten minutes to two hours, and were precipitated especially by emotional upsets. She was a well-built, healthy woman with an apparently normal heart. There were no signs of hyperthyroidism and the only focus of infection lay in some doubtful teeth which were removed later without influencing her attacks. Blood count, sedimentation rate, and X-ray of chest were all normal.

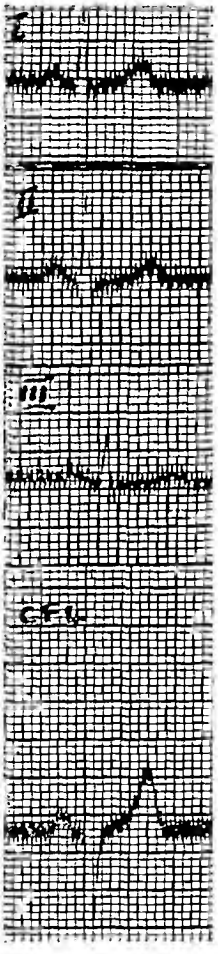

Fig. 1.—Sinus rhythm.

She was not unduly distressed during an attack of tachycardia; her pulse rate was 136, quite regular, and uninfluenced, clinically, by exercise or carotid sinus pressure. A triple venous pulse wave was visible at the root of the neck and the heart sounds were normal apart from their rapidity.

Electrocardiograms taken during sinus rhythm (Fig. 1) are normal in every respect. The P-R interval has been measured on numerous occasions and varies between 0·14 and 0·16 sec. Many records have been taken in the course of her paroxysms of tachycardia and practically no variation has been seen. The attack invariably starts with a premature P wave lying early in the descending limb of the preceding T; during the paroxysm P and T waves are superimposed and the sequence ends with a compensatory pause before the resumption of sinus rhythm (Fig. 2). The heart rate in these episodes is 136 and the P–R interval (which in this and subsequent records is measured from the summit of P to the summit of R) is slightly longer than in sinus rhythm, i.e. 0·16–0·18 sec.

Occasional isolated extrasystoles, which resemble the first beat of the tachycardia, have been observed and from the appearance of these complexes it would seem that the excitable focus must lie either in, or very close to, the S-A node.

Fig. 3 shows the first cardiogram obtained from the patient. In the limb leads the auricles are beating regularly at a rate of 152 whilst the ventricules have assumed an independent rhythm which varies between 113 and 136. The P waves in leads I and III are rather larger than those in records of sinus rhythm, and this, combined with the fact that their rate is greater than that in paroxysms of auricular tachycardia, may mean that a kind of flutter has developed. The QRS complexes are of supraventricular type and do not differ materially from those seen in other tracings, but the T waves are inconspicuous. The form and rate of the ventricular waves suggest that they arise in or near the A-V node. In CF_4 the rhythm is much the same as in the limb leads, but the auricular rate is a little slower and there may conceivably be conduction from auricles to ventricles, anyway after the first, seventh, and eleventh auricular contractions. CF_1, taken a few seconds later, opens with what seems to be the last beat of a paroxysm of auricular tachycardia; this is followed by two sinus beats, a short paroxysm of auricular tachycardia and finally by normal sinus rhythm.

The patient would not come into hospital for investigation and the following observations were therefore carried out in the out-patient department. They were kindly made for me by Dr. D. R. Humphreys working in Professor K. D. Wilkinson's clinic at the Queen Elizabeth Hospital, Birmingham.

Measurements reproduced in the various figures which follow are derived from naked eye examination without the aid of a comparator. They are therefore not strictly accurate but may serve to

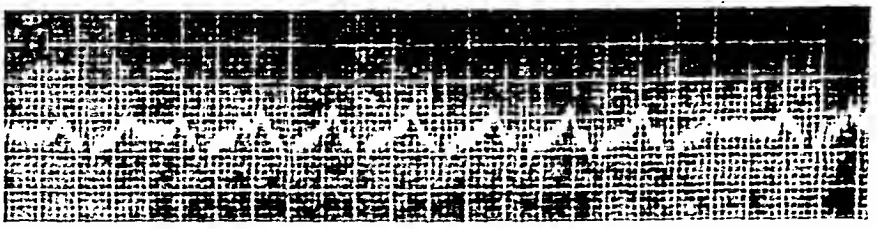

Fig. 2.—Onset and ending of a paroxysm of auricular tachycardia.

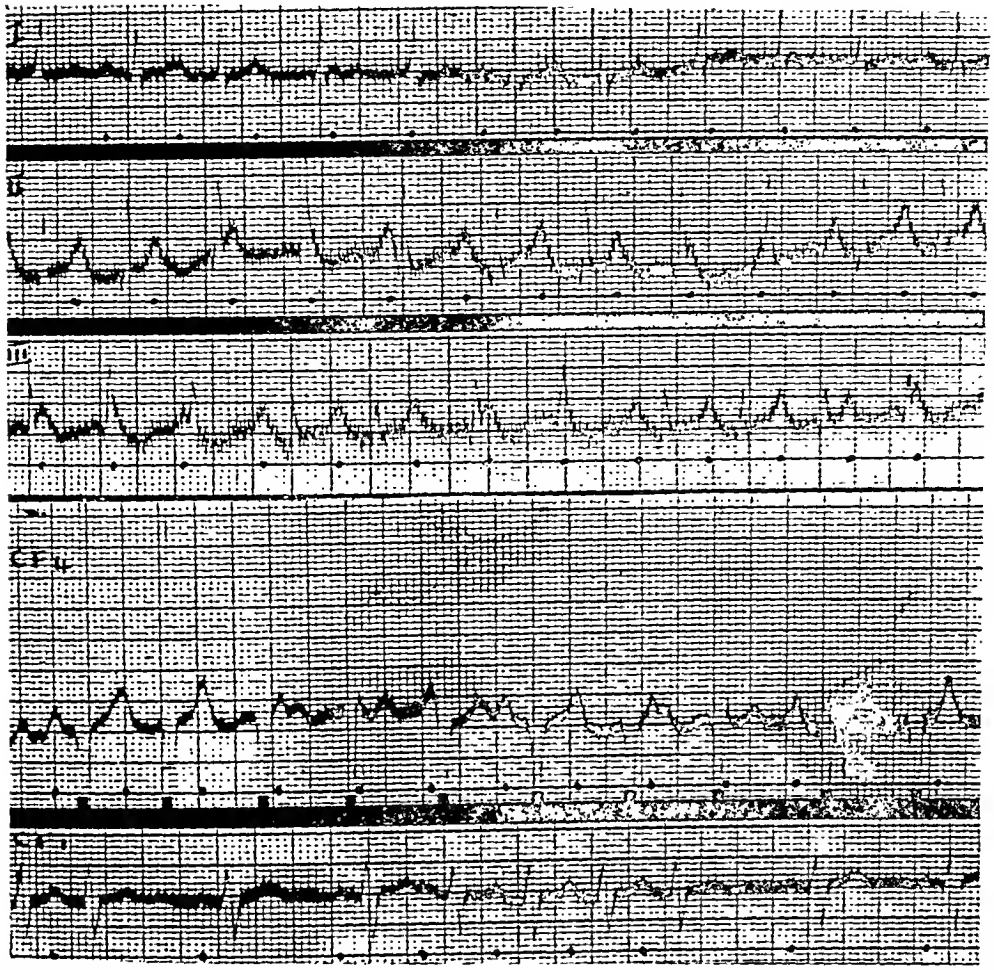

FIG. 3.—Cardiogram showing complete dissociation between auricles (marked with dots) and ventricles, in leads I, II, III, and probably in CF_4. CF_1 shows paroxysms of tachycardia and normal sinus beats.

emphasize the points brought out by the records. Exercise had absolutely no effect on the rate or form of a paroxysm of auricular tachycardia. Pressure on the left carotid sinus or on both sinuses simultaneously led to the resumption of sinus rhythm for a single beat (Fig. 4). The auricular rate continues practically unchanged whilst the ventricles beat more slowly. The last visible P wave before the sinus contraction is smaller than its predecessors, but it falls in front of, instead of on, a T wave and it does not differ materially from the P of the sinus beat. The next P wave is lost; it is perhaps directly superimposed on the QRS as the voltage of that complex is a little greater than the average. The T wave in the ventricular beat resembles that of the preceding complex, being much less conspicuous than its successor. The S–T interval is slightly depressed.

Lewis (1925) has pointed out that stimulation of the left carotid sinus will often decrease the speed of conduction from auricle to ventricle. If it is assumed that the missing auricular wave in Fig. 4 is buried in the ventricular beat, this may be an example of the Wenckebach phenomenon. The length of successive P–R intervals, measuring 0·16 sec. in the early beats, increases to 0·18, 0·30 and 0·39 before a beat is dropped and sinus rhythm is restored. The successive increments are therefore 0·02, 0·12 and 0·09, the first of which might perhaps be ignored. Further discussion of this subject follows later.

Five minutes after the sinus compression experiment, two minims of adrenalin (1 : 1000) were injected intravenously, in an attempt to stimulate the sympathetic. The patient became pale, shaky and apprehensive, with rather a feeble pulse. At the same time some interesting changes developed in the electrocardiograms. Fig. 5 is a section of the tracing taken immediately after injection. It shows two runs of tachycardia separated by a sinus contraction. The auricles continue to contract regularly at the paroxysmal rate of 136, whilst the ventricular rate slows. The last visible P wave in both of the abnormal sequences is small, but this can be explained by the fact that they are not directly superimposed on T waves (a small T is visible in the two beats before the sinus contraction). It is possible

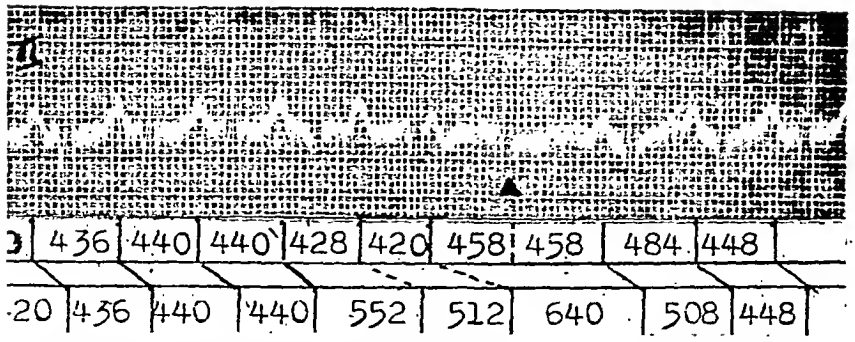

FIG. 4.—Effect of compression of the left carotid sinus during an attack of paroxysmal tachycardia.

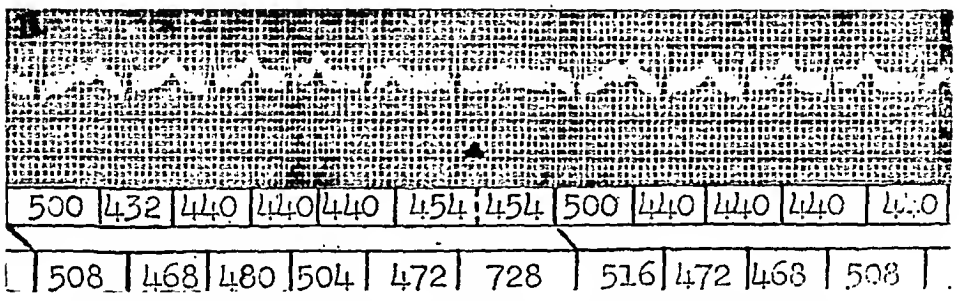

FIG. 5.—Paroxysm of tachycardia immediately after administration of adrenalin.

that a P wave falls on the final QRS of the first sequence, but if this is so the auricular contraction must be somewhat premature. The QRS waves in this tracing vary considerably in voltage but are obviously smaller than the average throughout. In other respects the record is not unlike an exaggerated version of that obtained by carotid sinus pressure.

Half a minute afterwards (Fig. 6), the same effect is still present, with the aurieles beating regularly

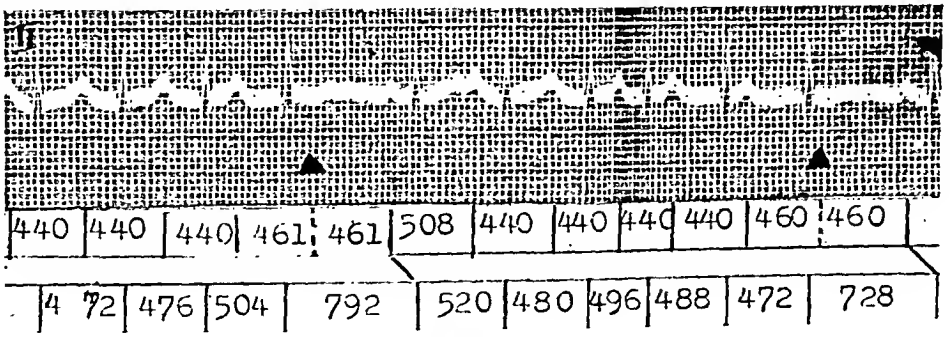

FIG. 6.—Approximately half a minute after adrenalin.

at a rate of 136 and the ventrieles lagging behind. The last P seen in the first sequence does not differ from those which go before it; presumably it is superimposed on a T wave. In the seeond sequenee the final P is of lower voltage, but it lies just before a small T wave. It should be noted that the third P wave of this sequenee differs in shape from the others beeause of a momentary stieking of the film in the camera. A reeurrenee of this meehaniеal defeet mars several parts of the eontinuous reeord taken throughout this experiment and makes measurements impossible in some plaees.

The seetion of film shown in Fig. 7 was taken about a minute after the exhibition of adrenalin and again demonstrates essentially the same features. By the end of the seeond minute (Fig. 8) the effeet of the drug is beginning to wear off, but the same tendeney is still reeognizable, the aurieles eontinuing at their old rate of 136 and the ventrieles beating rather more slowly. The shape and size of P waves is to all intents and purposes eonstant and for a P wave to be superimposed on the QRS before the sinus beat, considerable prematurity would be necessary.

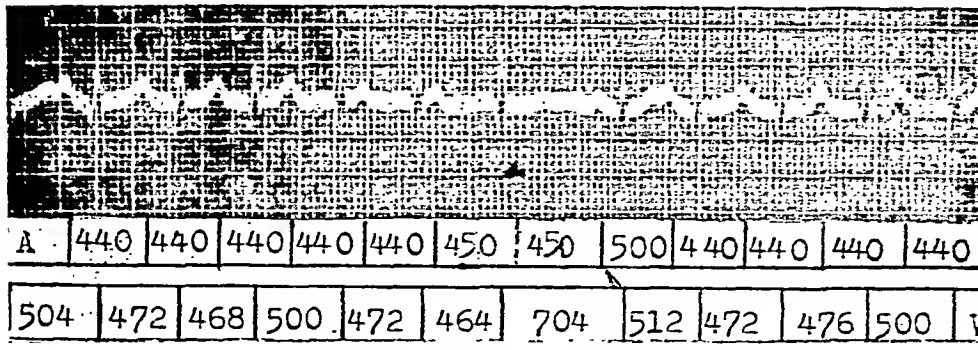

FIG. 7.—One minute after adrenalin.

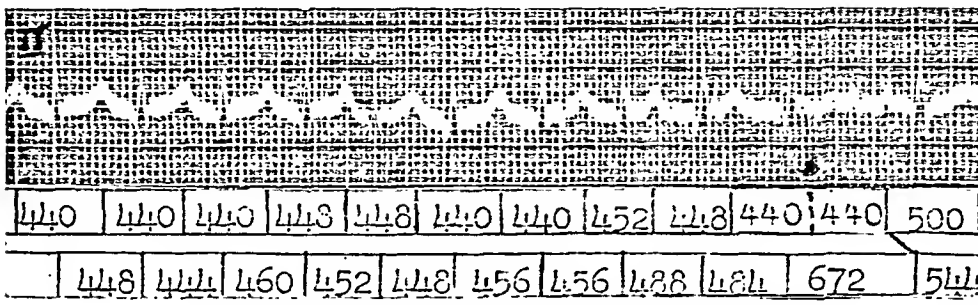

FIG. 8.—Two minutes after adrenalin.

Three quarters of an hour after giving the adrenalin an attempt was made to lower vagal tone by the injection of atropine (gr. 1/100) subcutaneously. Unfortunately the continuous film ran out at this point, but Fig. 9 (upper half) shows the state of affairs in lead I, 15 minutes later. The auricles

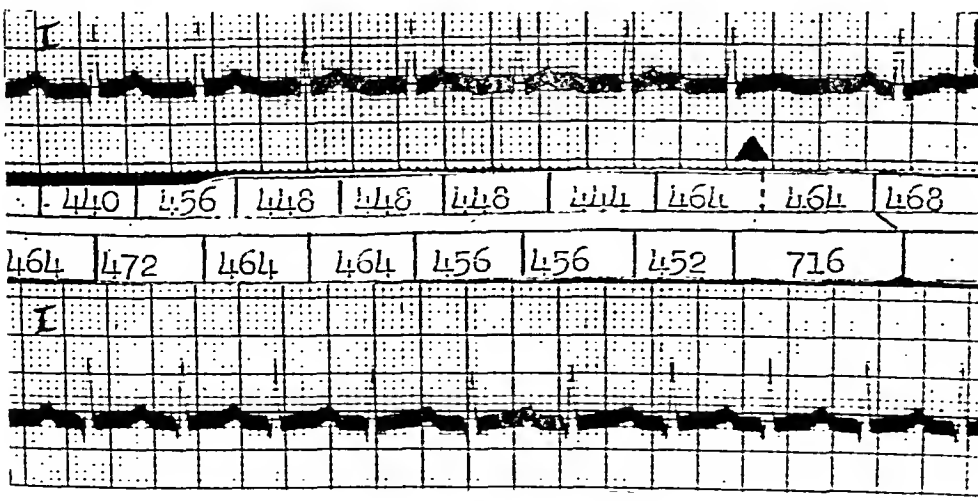

FIG. 9.—Twenty minutes after atropine.

are beating a little more slowly than in previous tracings but the ventricles are still slower than the auricles. The general features are the same as those already described after the injection of adrenalin, but in this film P and T waves are more readily distinguished. The QRS preceding the sinus contraction is not greater in voltage than the other waves of the curve and it seems unlikely that a P wave is incorporated in it. The sinus beat is followed by a premature P, lying in the descending limb of T, and almost certainly marks the initiation of the paroxysm of auricular tachycardia which is shown in the lower tracing, taken a few seconds later. The rate in this paroxysm is 141.

Discussion

Adrenalin, atropine, and probably carotid sinus pressure have all produced the same effect on a paroxysm of tachycardia. Lewis (1925) states that adrenalin, besides stimulating the sympathetic nerve endings, also acts directly on the vagal nerve centres in the medulla. Cushny (1936) agrees that the vagal centres may be stimulated, although he argues that it is not a direct action but a reflex stimulation following a rise of blood pressure. He points out too, as other writers have done, that atropine given in small amounts may activate instead of depressing the tenth nerve. It is probable, therefore, that the similar effects of all three experiments is due in each case to stimulation of the vagus.

It has already been observed that vagal stimulation may diminish the speed of conduction from auricles to ventricles. The Wenckebach phenomenon is characterized by three main features. The P–R interval progressively increases in length with each beat but the degree of lengthening decreases in successive complexes. Consequently the R–R intervals tend to become shorter and shorter until a beat is dropped. During the sequence auricular complexes are followed by ventricular complexes until the ventricle defaults, leaving an isolated P wave before the next sinus beat. Campbell (1943) has demonstrated, however, that the rule of P–R increments is not invariable and that occasionally the increase of the third interval over the second is greater than that of the second over the first.

Allowing both for Campbell's findings and for the fact that measurements taken from the tracings are not strictly accurate, it remains difficult to reconcile the figures (summarized in the accompanying table) with a diagnosis of partial heart block. Moreover in some of the cardiograms the R–R intervals tend to increase instead of diminishing with each successive beat.

Table Showing P–R Intervals and Increments Measured in Thousandths of a Second

Figure	P–R interval	Increment
4	160 ?180 308 392	?20 128 84
6a	180 208 248 308	28 40 60
6b	160 180 220 280 328 360	20 40 60 48 32
8	184 200 208 220 210 200 220	16 8 12 −10 −10 20
	240 260 308	20 20 48

The argument that partial heart block is responsible for the abnormal rhythm shown in Fig. 4–9 is in any case based on an assumption that seems quite unwarranted. It has been pointed out that in partial block the last wave before the sinus beat should be auricular. In none of the tracings is this final P wave visible and it has to be assumed therefore that it is superimposed on a QRS complex. This necessitates the further assumption that the quite regular auricular rhythm is broken, for in practically every instance the P wave would have to be slightly premature to fall directly on the QRS. Black triangles on the figures show the points at which the P waves would have fallen if the auricles had continued at their original rate. It is unbelievable that a premature P wave could fall with such exactness on a QRS on so many occasions. Consequently it is most improbable that this is an example of partial heart block with dropped beats, and if the condition is due to such a defect it is of most unusual type.

The changing shape of the P waves may suggest that there is a shift of the pacemaker towards the A-V node, but the alteration in size is also explicable by the relationship of the P and T waves, P being smaller only when the two fail to coincide. This is made the more probable explanation because in some of the tracings (Fig. 6 and 8) there is no change in the size of the P wave. The progressive lengthening of the P–R interval is a further argument against this diagnosis.

A third, and more probable, interpretation of the abnormal rhythm produced by vagal excitation is that there are short runs of complete A-V dissociation linked by isolated sinus beats. This would be in keeping with the spontaneous attack of dissociation illustrated in Fig. 3, especially if it is allowed that there are occasional sinus beats in CF_4. The development of the independent auricular and ventricular rhythms must be based on factors quite different from those which caused dissociation in White's (1916) case, or those mentioned by Hewlett (1923), for in the present instance the auricular rate continues unchanged and it is the ventricles that beat more slowly. It is likely that the auricles are driven by an excitable focus lying in or near the S-A node, a focus which is usually responsible for paroxysms of auricular tachycardia. In certain circumstances a barrier develops in the region of the A-V node, preventing the passage of impulses to the bundle. When this barrier is present the ventricular rhythm is probably governed by a second pacemaker lying in the neighbourhood of the A-V node. This pacemaker, having been sensitized to a high speed of activity by a paroxysm of auricular tachycardia, continues to send out impulses at a rapid rate, and so there develops a simultaneous auricular and nodal tachycardia.

Some light is thrown on the nature of the A-V nodal barrier by the effect of vagal stimulation during attacks of auricular tachycardia. The dissociation produced is then intermittent, with a sinus beat separating one period of block from the next. The sinus beat is always preceded by a dropped auricular beat. This suggests that the relatively long period of auricular inactivity allows sufficient recovery in the area around the A-V node for the next auricular impulse to follow its normal path to the ventricle. The passage of this solitary contraction wave again disarranges the mechanism and leaves a barrier which persists until the auricles once more default. The defect probably results from an abnormally long refractory period in the area concerned and is presumably related to the mechanism responsible for the Wenckebach phenomenon.

If the rhythm in all the records is in fact due to dissociation, it becomes difficult to decide at what point, following carotid sinus pressure (Fig. 4), conduction gives way to the two independent rhythms. It happens that this is the one electrocardiogram in which the Wenckebach phenomenon may be present, for it is easy to believe that the missing P is superimposed on a QRS. If, however, dissociation is present it probably develops at the fifth beat, where there is a sudden lagging of the ventricle. It will be noted that, as observed by Barker and his colleagues (1943), carotid sinus pressure fails to arrest the attack, but slows the ventricles.

Cardiograms not unlike the record in Fig. 3 were obtained from three of the patients described in Barker's paper (Fig. 7A, 8B, and 11B). These are considered to be examples of partial heart block, but the mechanism of impaired conduction is not discussed. The irregular rhythm of the ventricles is presumably ascribed to prolonged conduction from auricles to ventricles, but the variations in the P–R intervals are considerable and in the short illustrative tracings follow no obvious pattern, though such a pattern may perhaps be apparent in longer records. As far as can be seen the block is not of the Wenckebach type and is probably related to the mechanism described above. In this connection it is interesting that temporary nodal rhythm was observed in two of these cases. All three patients were receiving digitalis; two had organic heart disease and the third had an enlarged heart and, during attacks of tachycardia, a high blood pressure. The auricular rates in the illustrative records were 212, 188, and 167 with corresponding ventricular rates of 165, 112, and 131.

One other patient relevant to the discussion (Case 9) was a woman suffering from chronic rheumatic heart disease who, when under the influence of digitalis, developed tachycardia with partial block. Exercise increased the auricular rate slightly and " . . . the ventricles responded to each auricular beat for a short time, then became slower and irregular and finally displayed a long period of near standstill, interrupted by idiopathic ventricular beats. . . ." These idiopathic complexes are similar in structure to the complexes throughout the record, suggesting a point of origin close to the A-V node. This makes it clear that, in some cases of paroxysmal tachycardia, the auricular impulses may fail partly or completely to stimulate the ventricles, and that there is a tendency for the ventricles to be controlled by a pacemaker lying in or near the A-V node, the impulses from which are not necessarily regular.

On account of wartime conditions a thorough search of the literature has been impossible, but a limited review has revealed no other case in which the particular form of dissociation here described has developed in a patient without organic heart disease and not under the influence of digitalis.

SUMMARY

A case of paroxysmal auricular tachycardia is described, in which there developed a spontaneous attack of A-V dissociation, with high auricular and ventricular rates amounting to a double tachycardia. The condition could be partly reproduced during attacks of auricular tachycardia by atropine, adrenalin, and carotid sinus pressure. The patient's heart was otherwise normal and no drugs had been given. It is suggested that the condition is due to a form of heart block the mechanism of which is allied to, but not identical with, the Wenckebach phenomenon.

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PERSISTENT TRUNCUS ARTERIOSUS

BY

ROBERT MARSHALL

From the Royal Victoria Hospital, Belfast

Received August 1, 1943

A boy of thirteen years was first seen at his own home on April 5, 1943. A congenital heart lesion had been diagnosed early in life: he was undersized, but showed no other congenital defect; and there was cyanosis and clubbing of fingers. He was alert, intelligent, and engaging. For three days he had been vomiting blood in small quantities, but the total loss had been considerable. When first examined his heart rate was 144 a minute, the rhythm regular, and the pulse volume very poor. The apex beat was diffusely felt in the fifth space about two and a half inches from the mid-sternum; there was no thrill; there were soft systolic and diastolic murmurs audible all over the præcordium, but these murmurs proved to be transient.

On admission to hospital the hæmatemesis ceased, his pulse rate fell to normal, and no murmur could as a rule be heard, though sometimes there was an apical systolic bruit. Congenital methæmoglobinæmia as a contributory cause for his cyanosis was excluded. His blood pressure was usually 120/70. On April 19, his red cell count was 7,500,000 and his hæmoglobin 130 per cent. His temperature was unstable with a maximum of 100° F. Hæmatemesis recurred but never in alarming amounts. On April 28, his cyanosis was more intense, and gallop rhythm was present with a heart rate of 108, but this disappeared before his death from congestive failure on May 13.

The electrocardiogram showed large P waves in leads I and II; the S waves were approximately twice the amplitude of the R waves in leads I and III with splintering of QRS in II (Fig. 1).

An X-ray picture of the chest by portable apparatus showed " an enlarged globular heart of congenital type " (Fig. 2).

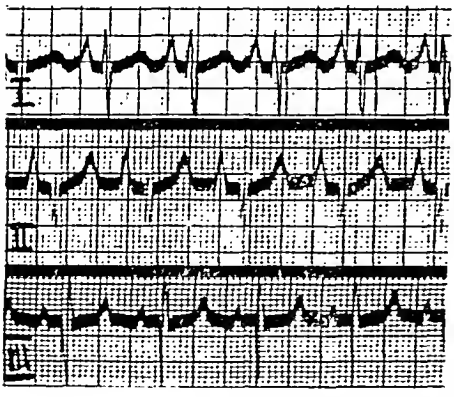

FIG. 1 and 2.—Electrocardiogram and radiogram (see text).

The transient murmurs made clinical diagnosis of the nature of his malformation difficult. The hæmatemesis was correctly attributed to œsophageal varices.

Necropsy Report

The heart was rather bulbous in shape. The longitudinal and transverse measurements being about the same—three and a half inches.

The transverse enlargement was entirely in the right ventricle, which completely covered the left ventricle when the heart was viewed from the front. The right auricle was very large and passed upwards and forwards in front of the aorta. The aorta was normal in appearance for its first one and a half inches and was only very slightly displaced to the right. There was no pulmonary artery arising from the right ventricle; instead a large arterial trunk arose from the left side of the aorta about one and a half inches from its origin (Fig. 3). This pulmonary trunk divided into a right and left artery after a course of about one and a half inches. The superior and inferior venæ cavæ emptied into the right auricle and the pulmonary veins emptied normally into the left auricle which was very small. The major branches of the aorta arose in their usual sites from the aortic arch.

The epicardium was normal and the sub-epicardial fat was considerable in amount. The veins in it were rather prominent.

On dividing the heart in its long axis through auricle and ventricle, the right auricle was found to be dilated and there was a large patent foramen ovale. The myocardium was hypertrophied, and the musculi pectinati were enormously hypertrophied. The auricular appendage between the musculi pectinati was very thin and almost transparent. The tricuspid valve was normal. The muscle of the right ventricle was hypertrophied and measured 2 cm. in thickness. The ventricular septum was slightly thicker. There was a complete absence of the membranous septum and the conus arteriosus was absent (Fig. 4). The blood must have passed through the deficient membranous septum to the aorta. The left auricle was very small and the myocardium was not hypertrophied. The mitral valve was normal and the left ventricular wall was slightly thicker than normal. The aorta opened from this

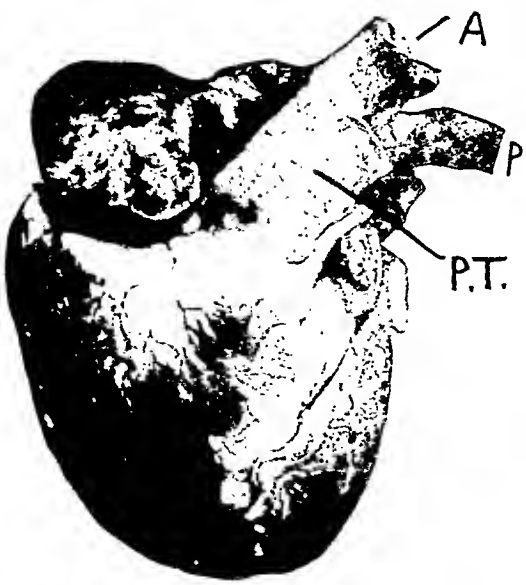

Fig. 3.—Anterior aspect of the heart showing enlarged right auricle and ventricle. P.T.=persistent truncus arteriosus. A=aorta. P=pulmonary artery.

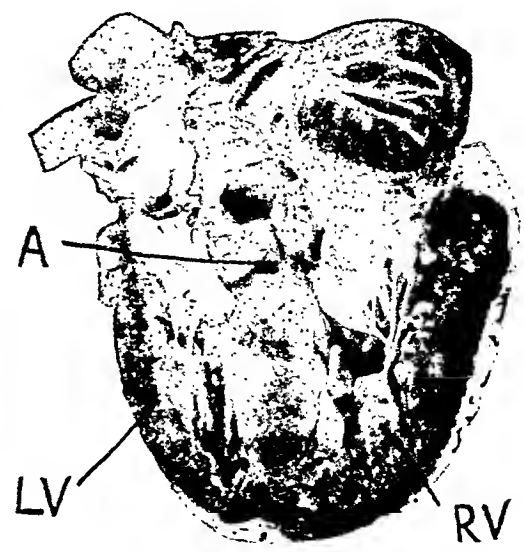

Fig. 4.—The heart on section, showing the absence of the pars membranacea of the interventricular septum.

ventricle and apparently the blood which reached it from the right ventricle did so through the deficient septum rather than because of dextroposition of the aorta. The aortic valve was tricuspid and competent; the cusps did not present a " fleshy " appearance and all the heart valves were free from endocarditis.

Comment

Of 1000 cases of congenital cardiac malformation analyzed by Maude Abbott (1932), 21 showed persistent truncus arteriosus; the oldest subject lived to twenty-five, but the average age at death was four years; hypertrophy of the right ventricle was found in 15 and of the left ventricle in 11 cases; dextroposition of the aorta was found in 19 cases. In the case now described it was at first thought that there was no dextroposition but on closer scrutiny it was considered that the truncus was slightly superimposed on the right ventricle and not altogether on the left. Brown (1939) agrees with Humphreys (1932) in describing five types:

(1) Partial common trunk with ductus arteriosus.
(2) Partial common trunk without ductus arteriosus.
(3) Complete common trunk with independent origin of pulmonary arteries.
(4) Complete common trunk with one pulmonary artery and a bronchial artery.
(5) Complete common trunk with no sixth arch derivatives and bronchial arteries.

The present case appears to be of Humphreys' fourth type, the single pulmonary artery arising as a branch from the common trunk and then dividing into right and left branches. Maude Abbott stated that four valve cusps of " fleshy " type are to be expected on embryological grounds but that tricuspid valves have been described in a number of cases including two of her own series. Brown quotes Ross (1935) that the cusps differ from normal cusps by the absence of elastic tissue and their general structure of myomatous tissue, and this finding was confirmed by Abbott. In the present case the three cusps were normal to both naked eye and microscopic examination.

Summary

A persistent truncus arteriosus was found after death in a boy aged thirteen years, who had always been cyanosed and breathless, and had suffered from hæmatemesis due to œsophageal varices. The cardiac murmurs had been transient; there was no endocarditis and death was attributed to congestive failure. Electrocardiogram, radiogram, and post-mortem findings are recorded.

I wish to thank Professor J. H. Biggart for his valued opinion, Dr. C. R. Murdock for the necropsy report, Dr. F. C. Montgomery for the radiogram and Mr. A. M. Mahaffy for photographs of the heart.

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COARCTATION OF THE AORTA, DOUBLE MITRAL A-V ORIFICE, AND LEAKING CEREBRAL ANEURYSM

BY

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From the University of Bristol

Received August 18, 1943

The purpose of this paper is to record and discuss the case of a boy with well-marked coarctation of the aorta, who made a complete recovery from subarachnoid hæmorrhage due to a leak from an intracranial aneurysm, only to die from rupture of a dissecting aortic aneurysm. A double mitral auriculo-ventricular orifice found at autopsy in this case is an extremely rare cardiac anomaly, only ten previous cases having been recorded (Abbott, 1927). In the present case the occasional diastolic or presystolic mitral murmur may have been the clinical counterpart of this anomaly. We can find only two previous cases in which recovery from a subarachnoid hæmorrhage in association with coarctation has been recorded—one in a girl, aged 12, reported by Lichtenberg and Gallagher (1933), and the other in a woman of 25, reported by Baker and Sheldon (1936)—and in neither case was the cerebrospinal fluid available for examination.

Clinical Features

The patient, R. W., was found to have abnormal heart sounds at the age of five years during a routine examination at a school clinic. He remained under observation, first of Dr. Carey Coombs and later of Professor Bruce Perry, until the age of 14, when he left school. During this period health and growth were normal and there were no relevant subjective symptoms. The cardiac lesion caused no apparent disability except that sometimes after exercise he became cyanosed. Its nature was not firmly established for some years. A loud apical systolic murmur was present constantly and it was noted that there was also from time to time another apical murmur which was mid-diastolic or presystolic in character; because of the latter murmur the possibility of a rheumatic origin was considered. From 14 to 17 years of age he worked in a factory, where his work included vigorous physical exertion, such as the moving of heavy packing cases: he had infrequent attacks of headache and vomiting. Later he worked as an A.R.P. messenger and he rendered good service during the air raids on Bristol. At the age of 17 years, on July 10, 1941 he had a sudden fainting attack, details of which are not available. On July 15, he had a severe attack of vomiting, lasting a few hours and followed, on the evening of the next day, by a sudden violent frontal headache attended by neck rigidity; this persisted until his admission to hospital on July 17, with a tentative diagnosis of acute meningitis. On examination in hospital the patient, a strongly built youth, had slow slurred speech and slow cerebration. Temperature and pulse and respiratory rates were normal. There was marked neck rigidity and Kernig's sign was positive on both sides, but there was no head retraction, and the abdominal and tendon reflexes were normal, and the plantar reflex on both sides was flexor. There were no signs of cranial nerve lesions, and the motor and sensory systems appeared normal. The cerebrospinal fluid was heavily blood-stained and under slightly increased pressure. 60 c.c. were withdrawn; three tubes were used to collect the fluid and in each the proportion of blood appeared to be about the same; it was free from clot. There was no relative increase in leucocytes; the protein was 20 mg.; chlorides, 760 mg.; and urea, 43 mg.; each per 100 c.c. On centrifugalization the supernatant fluid was quite clear and colourless.

Cardiovascular system.—The apex beat was very forcible and was situated in the fifth left interspace, one inch outside the mid-clavicular line. The first heart sound was completely replaced by a loud prolonged rasping murmur heard all over the præcordium. Pulsating vessels could be seen and felt in many areas of the chest wall, particularly, on both sides of the sternum, near the anterior axillary folds, over the upper part of the rectus sheath, and at the back between the inner borders of the scapulæ. A murmur similar to the cardiac murmur could be heard over many of the dilated super-

ficial arteries and was particularly marked just above and medial to the angle of the right scapula. The radial pulses were equal, full, and bounding, and the blood pressure in both arms was 220/120. The pulse in the femoral arteries could not be felt although a slight pulsation was felt in the left dorsalis pedis artery. The systolic blood pressure in the legs could not be determined accurately, the readings varying between 120 and 130; the diastolic pressure could not be determined. The lungs appeared normal and there were no other relevant findings.

On July 18 he was much better. The headache had gone. Slight ptosis of the left eyelid was observed. The cerebrospinal fluid was blood-stained, the pressure normal, the supernatant fluid straw-coloured, protein 25 mg., urea 43 mg., sugar 71 mg., each per 100 c.c. No relative increase of leucocytes, Wassermann reaction negative, culture sterile. A small quantity of cerebrospinal fluid was withdrawn twice daily for the next few days; the fluid became progressively clearer. On July 20 the neck rigidity had disappeared, the ptosis was diminished, and the speech somewhat improved. Radiographic examination showed an enlarged left ventricle and the characteristic notching of the ribs. No enlargement of the aortic arch could be seen. Progress continued satisfactorily and when he was discharged from hospital on August 16, 1941, he was mentally normal, his speech was normal, and there was no ptosis of the eyelid. At no time was there any elevation of temperature, pulse, or respiration. He seemed strikingly untroubled by his grave cardiac lesion and he presented the robust physique commonly associated with the so-called adult type of aortic coarctation. He returned to work and remained well, without headaches, for the next 13 months. He was, however, found dead in bed one morning, having died sometime during the night: he had felt perfectly well when going to bed on the previous evening.

Pathological Examination

The body was that of a well-nourished and well-developed youth. There were no external abnormalities. The serous cavities, with the exception of the pericardium, were normal, and the internal organs with the exceptions described below, appeared normal apart from a moderate acute congestion. The thymus weighed 45 grams.

Heart and Aorta. The main features were a supernumerary mitral valvular apparatus, a marked hypertrophy of the left ventricle, bicuspid aortic valves, fusiform dilatation of the ascending aortic arch with dissecting aneurysm and consequent rupture into the pericardial sac, almost complete coarctation of the so called adult type, and anomalous great vessels (Fig. 1).

The heart weighed 550 grams, mostly the result of a well-marked hypertrophy of the left

Fig. 1.—To show the coarctation, and the four vessels arising from the aortic arch. The arrow points to the rupture of the intima.

ventricle, the wall of which was 20 mm. thick. The left auricle appeared normal. The main mitral valve ring was 55 mm. in circumference. In the middle of its aortic cusp there was a complete accessory or supernumerary mitral apparatus, the ring of which was 45 mm. in circumference and furnished with two cusps which had a line of closure at right angles to that of the main mitral cusps. The accessory cusps were well supplied with chordæ tendineæ and papillary muscles; the cusps were well-developed, forming a narrow elongated cone (Fig. 2).

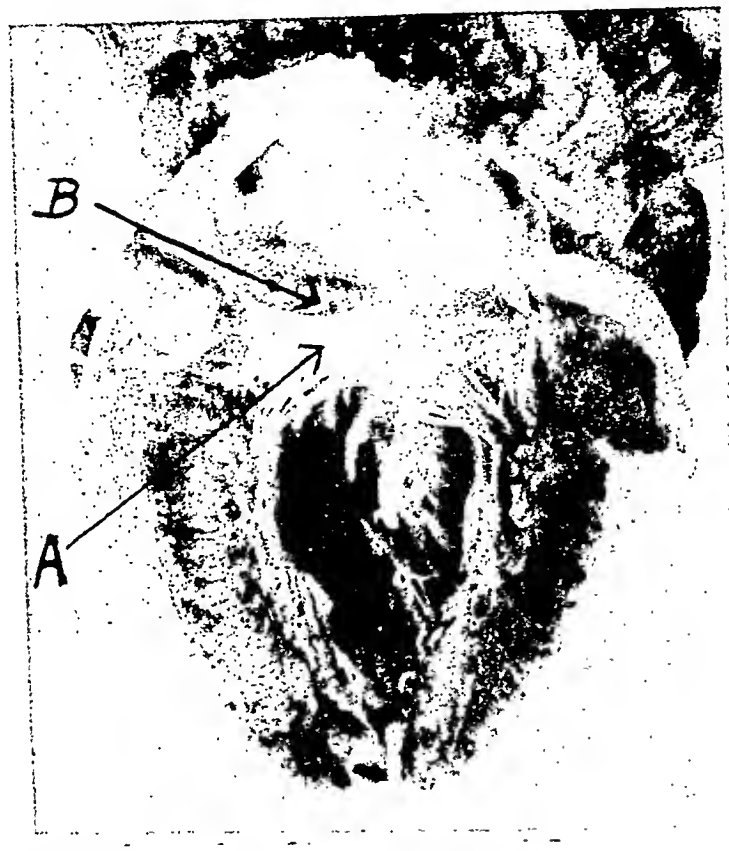

FIG. 2.—To show the double auriculo-ventricular mitral orifice, the left ventricle and the left auricle have been cut open and one cusp of the mitral valve divided and cut away. Facing is the aortic cusp of the mitral valve (marked A) with the supernumerary orifice: at the base of the opening (marked B) a small part of the left ventricular cavity can be seen.

There was no sclerosis or fenestration of any of the heart valves. The bicuspid aortic valves showed a slight diffuse thickening which rendered them more opaque than normal. The valve ring was 90 mm. in circumference. Both coronary arteries arose from the posterior cusp and there was no raphe in either aortic sinus. There were no other notable findings in the heart. The other measurements were: right ventricle, 5 mm. thick; circumference of the tricuspid ring, 100 mm., and of the pulmonary ring, 70 mm.

In the ascending aorta the fusiform dilatation showed a maximum circumference of approximately 130 mm., the aorta narrowing at the site of origin of the great vessels to a circumference of 25 mm. At the origin of the foetal isthmus there was a further considerable narrowing, the diameter showing a maximum of 5 mm.; the isthmus continued as a cone-shaped tube to the site of the coarctation, which admitted a hair-like probe after some manipulation. The site of the coarctation was at the attachment of the obliterated ductus. Below the coarctation the aorta rapidly widened to a circumference of 38 mm. The great vessels arose from the arch in four main branches which could not be traced out under the circumstances of the autopsy.

A dissecting aneurysm originated in a linear breach of the aortic intima, 35 mm. in length, and commencing 20 mm. above the posterior aortic cusp. The dissecting aneurysm extended, by a splitting of the media, from the root of the aorta to the origin of the great vessels to form a cuff-like sheath of blood. At a point in the aorta opposite the origin of the dissection the blood ruptured outwards into the pericardial cavity, resulting in a hæmopericardium, which was the immediate cause of death. Histologically (Fig. 3), at the site of origin of the dissection, there were numerous focal defects of elastic tissue in the media and the blood had ruptured

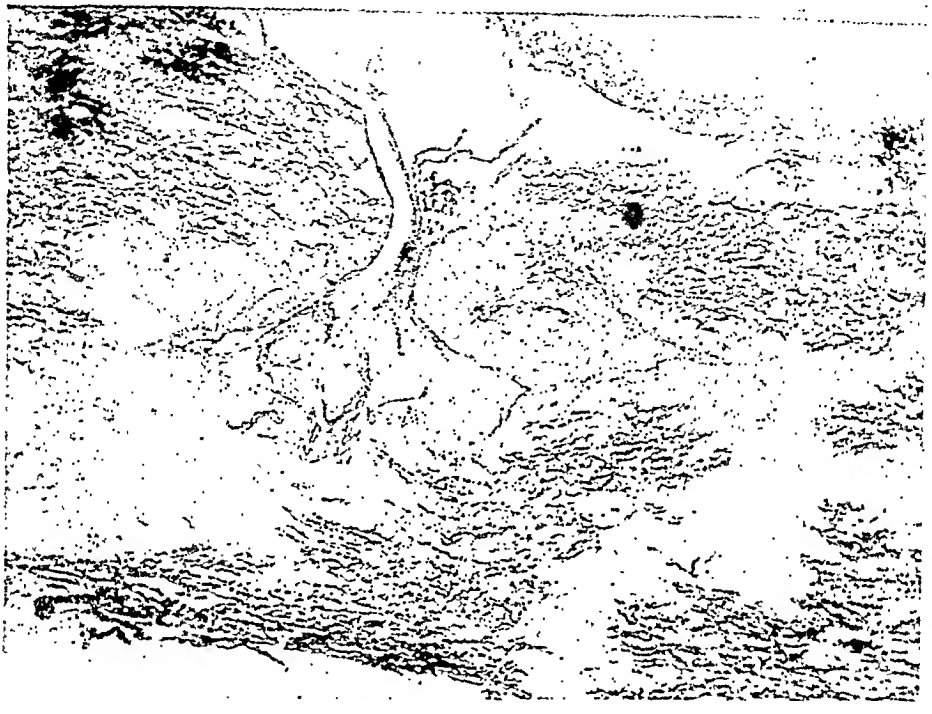

FIG. 3.—Aorta at the site of rupture through the intima, showing the beginning of the dissection. Magnification ×50.

through the intima into one of these breaches in the elastica. Similar focal defects with replacement by hyaline collagenous material were observed in sections taken from the ascending aorta in other sites and in a section from the aorta below the coarctation.

Below the coarctation the intercostal arteries showed considerable enlargement; at the orifices of these arteries there were a few smooth yellow patches of atheroma in the aortic intima. There was also an occasional yellow streak of intimal atheroma, both above and below the coarctation. There was no fatty intimal change at or near the origin of the dissecting aneurysm.

In the brain there was a berry aneurysm 1 cm. in diameter (Fig. 4), situated on the left middle cerebral artery just beyond its first main division as it passed on to the island of Reil. Above this berry aneurysm, about 4 cm. distant, there was a cyst in the brain substance which contained a faintly brown fluid. The cyst was about 2 cm. in diameter and the wall showed a deep yellow pigmentation. The adjacent pia-arachnoid showed a similar discoloration. No aneurysm could be identified in the small artery which passed into the wall of the cyst, but it appeared most likely that this lesion resulted from a leakage from a second ancurysm rather than from the aneurysm several centimetres distant. No other abnormalities were found in the brain or the meninges. Numerous sections of the arteries forming the circle of Willis were examined microscopically. Occasional defects of the muscular coat were observed of the type commonly found in normal subjects. Sections stained by Verhoeff's elastic tissue stain

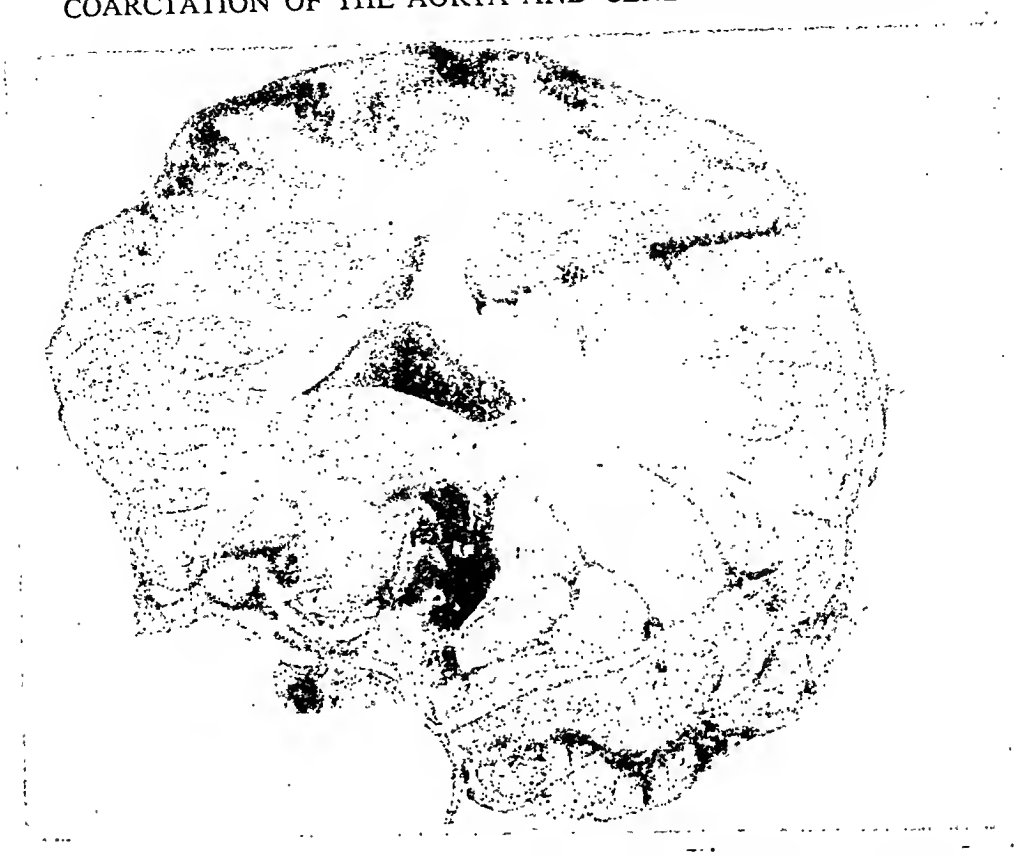

FIG. 4.—Cross-section of brain to show the aneurysm and the area of hæmorrhagic infarction.

followed by a modification of Masson's trichrome stain showed several irregularities and breaches in the internal elastic lamina reminiscent of the elastica defects in the aorta (Fig. 5). There was no atheroma of the cerebral vessels.

The left kidney weighed 200 g.; the right, 207 g. In both the capsule stripped easily leaving a smooth underlying surface. On section the normal architecture was clearly defined and there was moderate acute congestion. There was a normal proportion between cortex and medulla, the ratio being approximately 3 : 1. The main renal arteries appeared normal. Apart from acute congestion, no pathological change was observed. Several sections of the kidneys stained with Masson's trichrome stain were examined with the object of observing the Goormaghtigh bodies. No hypertrophy or hyperplasia of the Goormaghtigh cells was observed, and Lieut.-Colonel F. Bayless, U.S.A.M.C., kindly examined the sections and confirmed this observation. The small arteries and arterioles showed no muscular hypertrophy or other change.

DISCUSSION

The association between intracranial aneurysm and coarctation is an interesting one. Abbott (1928) considered that an intracranial aneurysm was most probably present in all cases of coarctation terminating with an intracranial hæmorrhage before the end of the second decade, where there was no history of infection or other apparent cause. She estimated that intracranial hæmorrhage was the cause of death in about 10 per cent of cases of the so-called adult type. In view of the high cephalic blood pressure in coarctation it is not surprising that recorded clinical cases of recovery from intracranial hæmorrhage with associated aortic coarctation are so very rare. In the present case the diagnosis of subarachnoid hæmorrhage was established by the finding of blood-stained cerebrospinal fluid. This fluid was obtained twenty-four hours after the onset of violent headache and neck rigidity, which was presumably the result of blood leaking into the subarachnoid space. The fluid showed an even

admixture of blood, with no clot and without variation in three successive samples from the first puncture, and the supernatant fluid was quite clear. Merritt and Fremont-Smith (1937) state that the cerebrospinal fluid will be yellow or xanthochromic if it has contained blood for more than four hours before removal. We consider that the evidence in this case is strongly in favour of the blood not being traumatic in origin and that it suggests that exceptions can occur to Merritt and Fremont-Smith's generally accepted statement. In the case under discussion subsequent specimens showed considerable hæmolysis.

An underlying factor common to intracranial aneurysm and aortic coarctation can now be considered in view of Glynn's (1940) observations on elastic tissue defects in intracranial arteries associated with aneurysm. Glynn directs attention to the importance of lesions of the elastic elements in the intracranial arteries in the genesis of these aneurysms, pointing out that the medial muscular defects can have little ætiological significance, occurring as they do in about 80 per cent of the population. He confirms that there is a peculiar concentration of the elastic tissue into the internal elastic lamina in the muscular cerebral arteries. From inflation experiments he shows that the unsupported internal elastic lamina can withstand a pressure twice as high as the highest recorded in cases of high blood pressure, and he suggests that the main strength of these vessels, concentrated as it is into one inner layer, is very susceptible to injury such as encroachment by atheroma; and he thinks it justifiable to conclude that this topographical peculiarity is also responsible for aneurysm formation as a result of non-atheromatous degeneration of elastic fibres. In view of Glynn's work we examined several serial sections of the circle of Willis in our case and found a considerable number of areas in which the internal elastic lamina showed a focal thinning or interruption, sometimes with replacement by hyaline fibrous tissue. An example of such a defect is illustrated in Fig. 5,

FIG. 5.—Breach of internal elastic lamina. Circle of Willis artery. Staining, Verhœff, and Masson. Magnification × 155.

and until we have the opportunity of examining an adequate series of normal cases to serve as controls we are unable to indicate their precise significance; but they are sufficiently striking to merit further attention, and they direct attention to a single pathological process which may be common to two anomalies having a marked clinical association, notably intracranial berry aneurysm and coarctation of the aorta. We consider that the weakening of the internal elastic lamina, which we believe existed in our case, is a condition similar in ætiology to the focal hyaline defects in the elastic tissue in the aorta. These defects were found microscopically in 12 out of 13 cases of rupture of the aorta reviewed by Abbott (1928), and they were present in our case above and below the coarctation (Fig. 6). There is no reasonable doubt

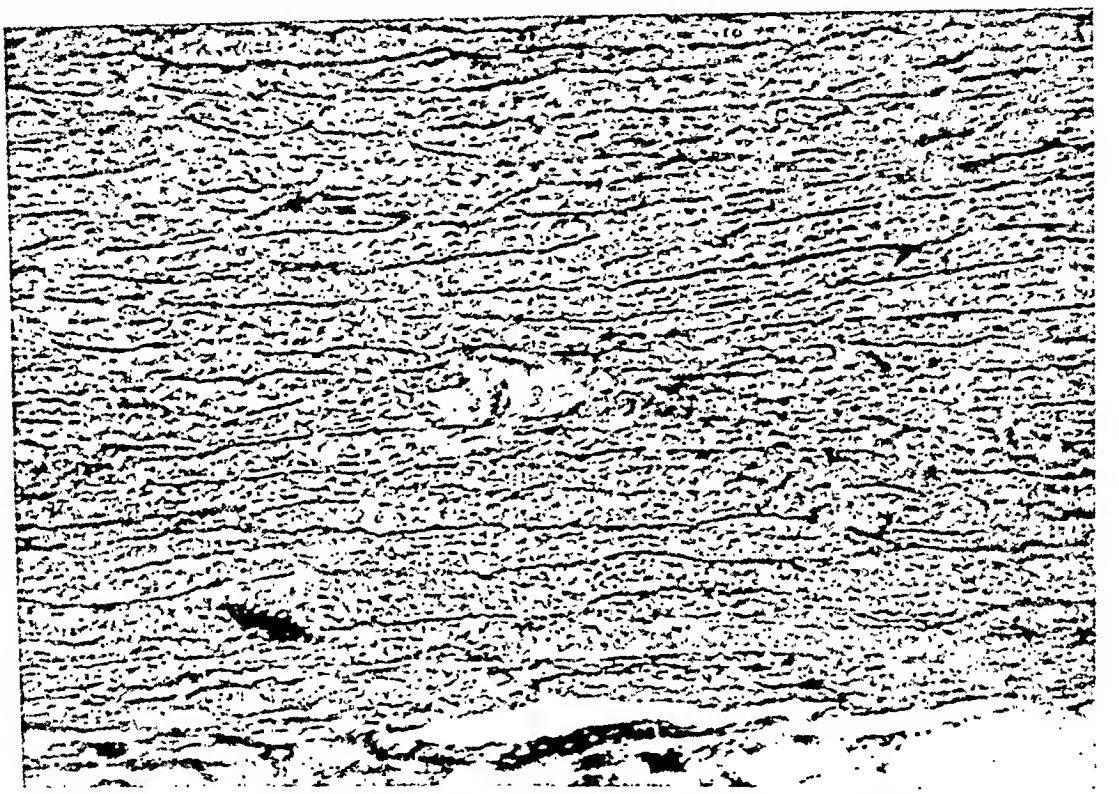

FIG. 6.—Elastica defects below the coarctation. Similar defects were shown in a micro-photograph above the coarctation, some distance from the point of rupture, but the figure has not been included. Magnification ×50.

that these defects in the aorta, congenital in origin, are the ætiological factor in the great majority of cases of aneurysm and rupture of the aorta associated with coarctation. They provide a striking parallel to the weakness of the elastica in the cerebral vessels. Shennan (1934) in reviewing 300 cases of dissecting aneurysm of the aorta decided that primary degenerative changes in the media were the most important factors and that some degree of stenosis of the aortic isthmus was not uncommon; in some of his cases there were symptoms suggesting a local lesion in the brain.

Clinically the occasional diastolic or presystolic heart murmur was possibly due to the supernumerary mitral valve. This murmur made it necessary at one period to consider the presence of rheumatic heart disease; that was, however, excluded at the autopsy. There is some obscure relationship between the aortic calibre and the presence of double mitral orifice for in two of the ten cases of double mitral orifice previously reported (Abbott, 1936) there was an associated aortic hypoplasia. The present case emphasizes this association, but we are unable to suggest any reason for its occurrence. Anatomical opinion that we have sought

considers that the two abnormalities cannot be explained satisfactorily on a single aberrant embryological process.

Summary

The case is reported of a male, aged 17, with coarctation of the aorta and other congenital defects. He developed a cerebral hæmorrhage from a berry aneurysm, and made a complete recovery from this, only to die later from rupture of the aorta.

The autopsy revealed that, in addition to the coarctation of the aorta and associated defects of elastic tissue, there was a double mitral valve. The probable counterpart during life of this rare anomaly was a presystolic or diastolic murmur in the mitral area.

The relationship of these defects is briefly discussed.

We wish to thank Professor C. Bruce Perry for his clinic notes and Mr. T. J. H. Cooke who took the photographs.

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TRIPLE HEART RHYTHM*

BY

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Triple heart rhythm stands for the cadence produced when three sounds recur in successive cardiac cycles, just as two sounds compose the familiar dual rhythm of cardiac auscultation, and more rarely, four sounds a quadruple rhythm.

The conflicting views on the subject have long served to discourage attempts at a clinical perception of the problem. Disagreement is perhaps best illustrated by recounting the varied terminology employed to describe it. Thus we have gallop rhythm, canter rhythm, and trot rhythm; presystolic gallop, systolic gallop, protodiastolic gallop, and mesodiastolic gallop; complete summation gallop and incomplete summation gallop; auricular gallop, ventricular gallop, and auriculo-ventricular gallop; true gallop; left-sided gallop and right-sided gallop; rapid-filling gallop; diastolic echo; mitral opening snap; reduplication of first sound and reduplication of second sound; Potain's murmur; third heart sound and fourth heart sound. Others may have escaped my notice. This muddled nomenclature, as long as it stands, will frustrate any attempt to unify the many views held on triple rhythm. There is need of a simplified terminology based on clinical findings. It is indeed clear that a neglect of the clinical aspect on the one hand, and a persistence on the part of many to explain the *mechanism* of the supernumerary sound on the other hand, and to classify triple rhythm in accordance with sound records, have been largely responsible for obscuring this common form of cardiac rhythm. Phonocardiography need not become a routine test in clinical cardiology; when it has helped to establish a classification of triple rhythm it will have achieved its main purpose, though it will still serve in other auscultatory problems. In the present investigation it has been a condition that the supernumerary heart sound should be elicited first by clinical auscultation. No phonocardiogram was taken as a preliminary test, and it was only recorded later in order to confirm or correct the clinical impression that had already been gained.

Among patients attending the Cardiac Department of the London Hospital during a recent period, and known to have heart disease or referred for an opinion on the heart, there were 270 who presented triple rhythm. These were placed in a special series for which a set method of inquiry had been prepared. A regularized history was taken and a general examination was made. A special record was taken of the heart rate at rest and after exercise, the presence of cardiac enlargement, the symptoms and signs of heart failure, and the blood pressure. As to the supernumerary sound, its site, distribution, and character, were separately noted, as well as the effects upon it of respiration, change of posture, and induced tachycardia. The apical impulse was examined by palpation and direct auscultation. Cardioscopy was a routine method of examination by which the size of the separate heart chambers was assessed. At the start certain measurements were taken; these included the width of the heart and thorax, and the height of the right auricle and diaphragm, but they were discontinued when it was realized that they brought no valuable information. Sometimes, however, use was made of

* The third Strickland Goodall Memorial Lecture delivered before the Worshipful Society of Apothecaries in London, June 24, 1942.

the distance between the junction of the right auricle and superior vena cava and the summit of the pulmonary arc, for it partly expressed the degree of pulmonary artery distension when present. In certain patients a limb lead electrocardiogram was always taken. A phonocardiogram by a Cambridge string galvanometer and the electrocardiogram were taken simultaneously on the same plate.

In addition to the series of patients with triple rhythm, 200 subjects were added in due course to serve as control cases for this investigation of certain types of triple rhythm.

Classification

I do not intend to deal here with a complete bibliography of the subject because a faithful account of it was recorded by Holt (1927). Of course I shall refer to the work of many of those who before and since have described their clinical and graphic findings in patients with triple rhythm, and have thus contributed much to our knowledge of the problem. Particularly do I want to mention the astute observations of Potain (1856, 1866, 1876, 1880, 1894, and 1900) in pre-phonocardiographic days more than half a century ago. He differentiated between gallop and split sounds. A reduplicated or split sound, he said, was one where the two components had the same quality and pitch and were separated one from the other by a very short interval, while a gallop rhythm had a sound added to the normal sounds, and separated from them by an appreciable interval. The added sound was usually short and dull, a sort of thud, often better felt than heard, and frequently missed if auscultation was carried out with a stethoscope alone, monaural though it was. Usually it was detected in the region between the apex, the left border of the sternum, and the second rib, and it was sometimes heard over a limited area. The added sound was always diastolic and according to its position it could be described as protodiastolic, mesodiastolic, or presystolic. The typical gallop was presystolic; the protodiastolic gallop presented a diastolic echo and could be likened to the recall on the drum or a rebound of a hammer on the anvil.

The term gallop rhythm has become rooted in the history of triple heart sounds and most writers have adopted it. But since the qualifying terms gallop and canter only imply that the rhythm initiated by three sounds in the cardiac cycle is simulated by the sounds produced by a moving horse, and since adherence to such terms prevents a modern understanding of this form of cardiac rhythm, I mean to discard them. Instead it is only necessary to appreciate that when a supernumerary sound in the cardiac cycle gives rise to triple rhythm, three types may be recognized according to the position of the adventitious sound.

In the *first type* the added sound is found early in cardiac diastole; it follows the second sound immediately and is the third sound in the cardiac cycle. In the *second type* the added sound occurs late in ventricular diastole; it succeeds the period which the third sound customarily occupies, immediately precedes the first heart sound, and therefore may be styled the fourth sound. Thus the third sound disturbs the early part of the silent diastolic period, and the fourth sound disturbs the end part. In the *third type* the added sound is situated towards the end of systole just before the second heart sound. The position of the adventitious sound in the respective types is usually determined readily by auscultation even in the presence of moderate tachycardia. Severe tachycardia may be a distinct handicap although even then a classification of triple rhythm can usually be determined, and especially when aided by ancillary clinical data, but short of phonocardiography. A scheme setting out the positions occupied by these supernumerary sounds in the cardiac cycle is shown in Fig. 1.

The clinical conditions which give rise to the supernumerary sounds have been arranged according to the type of triple rhythm which they constitute, and this arrangement suggests a classification of triple rhythm.

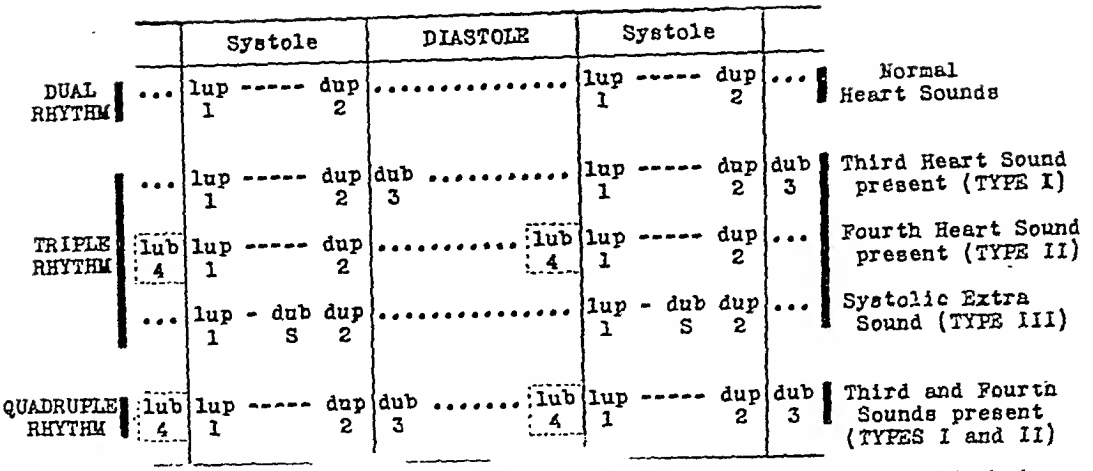

FIG. 1.—Scheme showing position of heart sounds in cardiac cycle in different types of triple rhythm. S—systolic extra sound. Fourth heart sound occurs in *ventricular* diastole, but in *auricular* systole.

TABLE I

THE CLASSIFICATION OF TRIPLE HEART RHYTHM

	No. of cases	
Type I.—Addition of the third heart sound		205
(*a*) In health	125	
(*b*) In right ventricular failure	80	
Mitral stenosis	44	
Hypertension	16	
Thyroid toxæmia	8	
Congenital heart disease	7	
Emphysema	5	
Type II.—Addition of the fourth heart sound		60
(*a*) In delayed A-V conduction	14	
(*b*) In left ventricular failure	46	
Hypertension	41	
Aortic incompetence	5	
Type III.—An extra heart sound in late systole		5
Total 270 cases		

The special clinical and graphic features of the three types of triple rhythm will now be described.

TYPE I.—ADDITION OF THE THIRD HEART SOUND

When the third heart sound becomes audible in successive cardiac cycles, a form of triple rhythm designated here Type I, is established. As long ago as 1855 Stokes reported a case in which an early diastolic sound was heard, but it was A. G. Gibson (1907) and Hirschfelder (1907) who independently discovered that a wave in the venous tracing was associated with a sound in early diastole. Gibson found that this " b " wave, placed between the " v " and " a " waves, was seen at its best in healthy young adults, and in two of these he detected a sound between the second and the succeeding first sound. He said that it was not easy to hear, but was most distinct in the short interval between expiration and inspiration, and when pressure was applied to the abdomen. Gibson informed Einthoven of his discovery and the latter (1907) recorded a sound which corresponded in position with Gibson's " b " wave and Hirschfelder's " h " wave.

I have assembled 205 cases that on clinical examination showed triple rhythm due to the appearance of the third heart sound. Of these 125 were healthy subjects, while the remaining 80 had some form of heart disease.

Before defining the precise position of the third sound in the cardiac cycle it is necessary to describe the normal phonocardiogram of dual rhythm and the relation of the separate phases of the tracing to the electrocardiogram. Thus, the auricular sound in health starts, as a rule, at the end of the P wave and merges into the ventricular part of the first sound which

starts near the S wave and never in front of the R wave. The second sound begins at the end of the T wave (Fig. 2).

Type Ia.—The Third Heart Sound in Health

Einthoven (1907) found that the third heart sound in healthy subjects commenced 0·10 to 0·15 sec. after the onset of the second sound, and Lewis (1912) confirmed this. The average in my series was 0·19 sec. (Fig. 3). I have found no value in the measurements which express

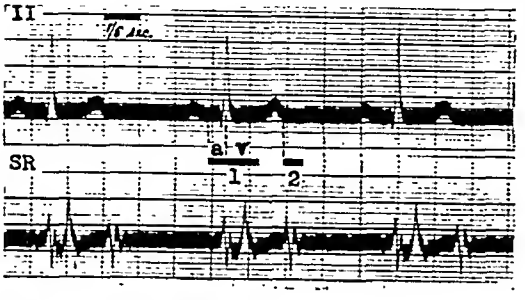

Fig. 2.—Dual rhythm. Healthy man, aged 25. In this and subsequent figures, SR is sound record, and a and v are auricular and ventricular parts of first heart sound respectively.

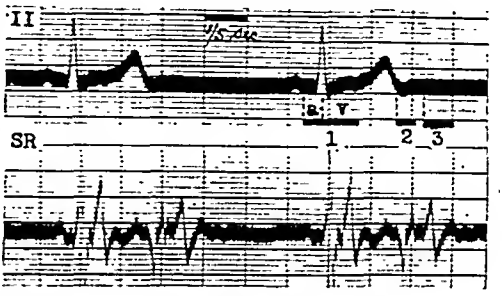

Fig. 3.—Triple rhythm, Type Ia. From a healthy man, aged 21.

the duration of the supernumerary heart sounds, but the measure of the interval between them has great value. Thus it is not unusual for this interval to become annulled and cause the third and fourth sounds to fuse from shortening of the diastolic phase by tachycardia and/or lengthening of the auriculo-ventricular period.

Mechanism. As it is of no consequence here to know the actual mechanism producing the third heart sound, little time will be spent in debating the many theories advanced to explain it, for our closest attention needs to be directed to the clinical data presented by subjects with this form of triple rhythm. It is sufficient, therefore, to recount the common views. Gibson (1907) thought that sudden distension of the ventricle by blood from the auricle accounted for the sound, implying vibration of a taut ventricular wall. Einthoven (1907) believed that it was caused by vibration of the semilunar valves. According to Thayer (1908) and Sewall (1909) the sound is produced by vibration of the auriculo-ventricular valves after they have been floated into a position of closure by blood distending the ventricles. Thus, it is not known for certain which part of the heart vibrates, but this is immaterial for a clear understanding of the more noteworthy clinical aspects.

Incidence. The incidence of this type of triple rhythm is commonly regarded as uncertain, for while many writers speak of it as a common clinical finding, others have said it is rare and some have disputed its existence. Obrastzow (1905) heard it in 90 per cent of healthy subjects, Thayer (1909) in 65 per cent of healthy young adults, Gubergritz (1925) in 93 per cent, and Steinberg (1925) in 95 per cent of healthy children. Bridgman (1915) heard the sound in 13 out of 15 healthy boys, aged 12 to 15 years, and recorded it phonocardiographically in all of them. The third heart sound was recorded in 60 out of 100 medical students in whom sound tracings were taken by Braun-Menendez and Orias (1934).

When 50 control cases with dual rhythm were collected alongside 50 subjects showing a third sound, triple rhythm was commoner than dual rhythm in subjects of 15 to 18 years of age, and only a little less common between the ages of 18 and 20. A general acceptance of the fact that this form of triple rhythm is so common in young subjects is overdue. This realization will come to us as soon as we regularize auscultation to include self-catechism having as one of its questions: " Do I hear more than two heart sounds?" Reference to the incidence of this type of triple rhythm in older subjects is scarce. Since this has an important

bearing on differential diagnosis from other forms of triple rhythm, I sought it at all ages. Its rare appearance in older subjects became apparent. In a series of 125 where this form of triple rhythm was heard, which excluded children under 9, 115 were under 25 years. The actual incidence among the older group was as follows: 1 aged 25, 1 aged 26, 1 aged 27, 1 aged 28, 2 aged 30, 1 aged 34, 1 aged 35, 1 aged 38, and 1 aged 39. Thus triple rhythm, Type Ia, was never heard in subjects of 40 or over; it was rare over 30 (4 out of 125) and uncommon at 25 or over (10 out of 125).

Site. The third heart sound was best heard in the fourth intercostal space at a point half-way between the nipple line and the lateral border of the sternum and, therefore, a little way internal to the mitral area (Fig. 4). In two patients in whom the sound was more distinct

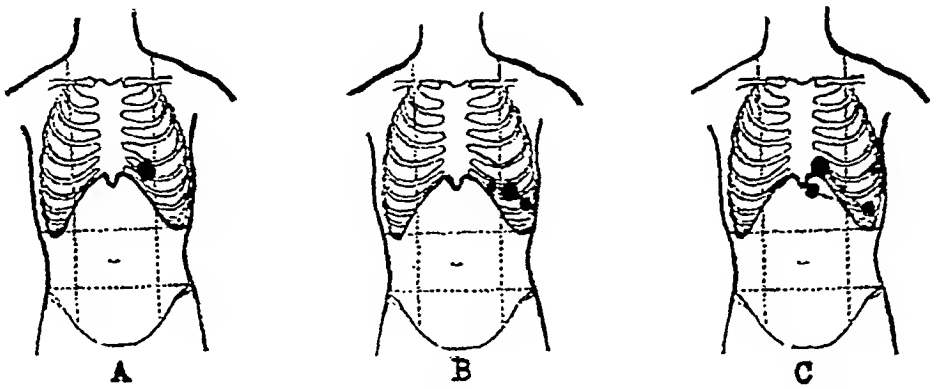

FIG. 4.—Localization of supernumerary sounds in triple rhythm. Dots and discontinuous lines indicate places of maximum intensity and distribution. (A) Type Ia, Type IIa, and Type III. (B) Type Ib. (C) Type IIb.

just outside the mitral area, the heart was found to be displaced outwards by scoliosis. The location of the sound is important because it may by itself decide the diagnosis of triple rhythm Type Ia (third heart sound in health) from Type Ib (third heart sound in disease), for in the physiological variety it is most distinct inside, and in the pathological type usually outside, the mitral area. In part, perhaps wholly, this variation in the site of maximum intensity of the sound in the two groups depends on the size of the heart, so that in the pathological states which may show a third heart sound, the apex beat is moved outwards from cardiac enlargement.

Conditions influencing the intensity of the sound. In order to bring out the third heart sound or to increase its intensity, Thayer (1909) adopted certain manœuvres which moved the apex nearer to the chest wall and accelerated the venous return to the heart. Thus he listened with the subject in the reclining posture after exercise, or inclined on his left side, or while an assistant elevated the arms and legs; he also applied abdominal pressure. I have tested all these means and found that only two consistently accentuated the third heart sound, namely the induction of moderate tachycardia, and the adoption of the reclining posture. In all 125 subjects with triple rhythm, Type Ia, the sound was best heard in the reclining posture, and in 90 the sound actually disappeared as the subject assumed the upright position. In 22 of the 35 cases in which the sound persisted in the upright posture, its audibility only lasted as long as the tachycardia induced by the change of posture lasted.

The influence of posture on this triple rhythm also helps materially to decide which variety is present, whether Type Ia or Type Ib. This in Type Ib the third sound is heard in both upright and reclining postures, whereas in Type Ia the sound usually disappears in the upright posture unless tachycardia is present (Fig. 5). Presumably this characteristic influence of posture is related to pressure within the right heart so that in the pathological type of triple rhythm the increased pressure does not fall below the threshold at which the third sound appears, even when the upright posture is adopted.

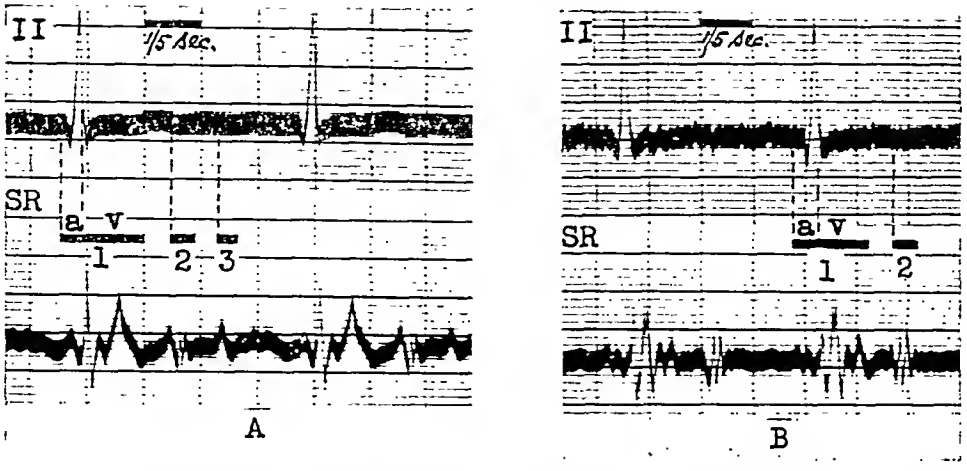

FIG. 5.—Triple rhythm, Type Ia. The third heart sound recorded in the reclining posture (A) disappeared in the erect posture (B). From a healthy girl, aged 15.

The Heart in Triple Rhythm, Type Ia

From routine cardioscopy in healthy subjects with a third heart sound, I found that the heart showed a characteristic outline. My early impression was that its most distinctive feature was enlargement of the pulmonary artery seen as a prominent pulmonary arc. Thinking that this might be part of a more general distension of the right heart I sought other signs, so that the height of the venous column in the neck was measured, and at cardioscopy a record was made of the size of the right auricle and ventricle, and prominence of the superior vena cava and hilar shadows; the height of the diaphragm and of the right auricle was measured as well as the width of the heart and thorax. Although these changes were not found consistently, yet some characteristic of the average radiological appearance of the heart in young subjects was very often preserved. Thus, there might be a squat-like appearance of the cardiac shadow, high diaphragm and shallow thoracic cage, prominence of the right auricle and sometimes of the superior vena cava, prominence of the pulmonary artery which filled the pulmonary bay, and increased density of the hilar shadows (Fig. 6). As enlargement

FIG. 6.—Characteristic heart outline in healthy child, aged 12. Pulmonary artery index (hereafter designated P.A. index), 6·0. This and subsequent X-rays are teleradiograms.

of the pulmonary arc was the most constant feature of the cardiac silhouette, a search was made for a means of recording the impression of the size of the pulmonary artery obtained by cardioscopy. For this purpose the distance was measured between the junction of superior vena cava and right auricle, and the summit of the pulmonary arc. This distance, measured in centimetres, is a rough estimate of the degree of pulmonary artery distension and I have named it the *pulmonary artery* (*P.A.*) *index* (Fig. 7). This value, representing as it does the width of the vascular pedicle at its base, is not an actual measure of the pulmonary artery, and two facts lessen its usefulness; the distance is increased by elevation of the diaphragm and diminished when the diaphragm is low, and the measurement is increased to the right when the ascending aorta is displaced from unfolding of its arch. Yet I have found the measurement useful as a means of recording the visual impression of the size of the pulmonary artery, although the numerical value does not always tally precisely with the judgement formed on cardioscopy which must remain as the most dependable guide in this matter.

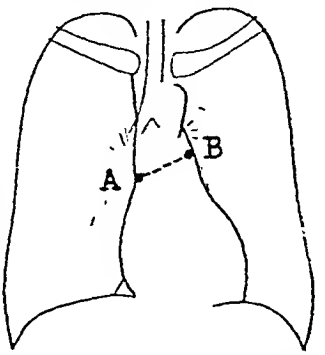

FIG. 7.—Measure of pulmonary artery distension. A, junction of superior vena cava and right auricle. B, summit of pulmonary arc. Distance AB in centimetres is *pulmonary artery* (*P.A.*) *index*.

In 50 consecutive cases over the age of 15 the size of the pulmonary artery was estimated in terms of the pulmonary artery index as well as by visual impression, and was compared with the same findings in 50 subjects of corresponding age presenting dual rhythm. In the triple rhythm series the artery was prominent in 47 as against 8 in the control group with dual rhythm (Fig. 8). In 2 cases showing prominence of the pulmonary artery (moderate in one, and conspicuous in another) in which the third heart sound was not heard by clinical auscultation, the phonocardiograph recorded the sound. Although some degree of pulmonary artery enlargement was found in a few cases (8 out of 50) in which no third heart sound was heard,

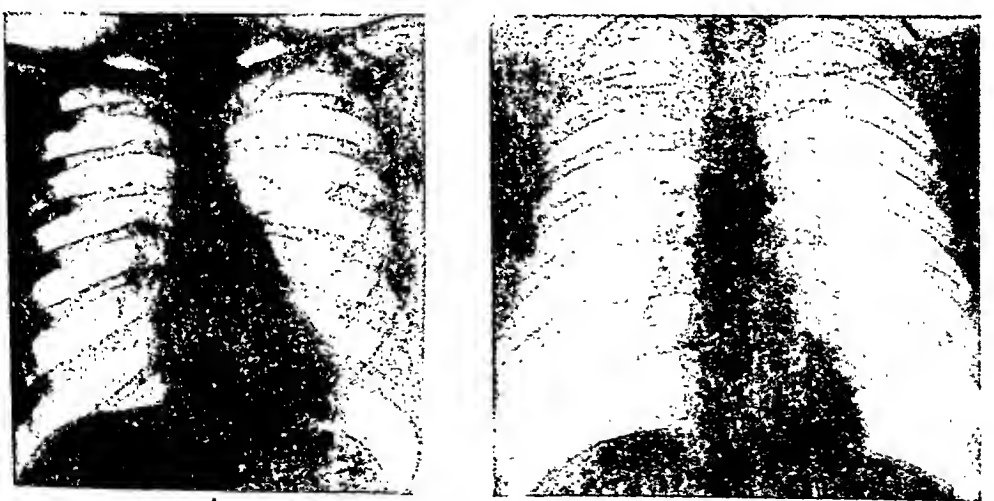

FIG. 8.—Triple rhythm, Type Ia. Teleradiograms in two healthy subjects, aged 23. (A) with a P.A. index of 6·8 showed triple rhythm and (B) with a P.A. index of 6·1, dual rhythm. Other similar contrasted pairs were submitted but had to be omitted from consideration of space.

and no enlargement in 3 of the 50 cases in which the third heart sound was present, the incidence of this radiological finding was so common in the triple rhythm group compared with the control group with dual rhythm, that the association between pulmonary artery enlargement and triple rhythm, Type Ia, is strongly supported. I have been at some pains to

control the observation, and it is significant that 40 out of 50 cases with triple rhythm showed a pulmonary artery index of 6·5 or over, whereas the index was less than 6·5 in 41 out of 50 cases of the same age that showed dual rhythm (Tables II and III). The limb lead electrocardiogram in subjects in this group was in no way distinctive, but changes in the chest leads are being further examined.

TABLE II

THE SIZE OF THE PULMONARY ARTERY IN 100 HEALTHY SUBJECTS HALF WITH TRIPLE RHYTHM (TYPE Ia) AND HALF WITH DUAL RHYTHM

Age	Estimate of pulmonary artery distension at cardioscopy		Pulmonary artery index	
	Subjects with triple rhythm	Control cases	Subjects with triple rhythm	Control cases
16	+ + *	— *	7·0	5·5
16	+ +	—	7·0	5·9
16	+ + +	—	7·0	5·5
17	+	—	6·5	5·0
17	+	—	7·0	6·0
17	+ +	—	6·5	5·7
17	+	—	7·0	5·2
17	+	—	6·0	5·0
18	+ +	—	7·0	6·0
18	+	—	6·5	6·5
18	+ +	—	7·0	6·4
18	+	—	6·5	6·0
18	+	—	6·4	6·4
18	+	—	7·0	5·9
18	+ +	—	6·5	5·0
18	+ +	—	7·0	5·6
18	+	—	7·0	5·7
18	+	—	6·5	5·5
18	—	—	5·5	6·2
18	+ + +	—	8·0	6·4
18	+	—	6·5	5·4
18	+	+	6·0	6·1
18	+ +	—	6·8	5·3
18	+ +	+	7·2	5·5
18	—	—	6·2	5·5
19	+ +	—	7·0	5·8
19	+	+	6·0	6·5
19	+ +	—	7·0	5·5
19	+ +	—	7·0	4·5
19	+	—	6·5	6·2
19	+ +	—	7·0	5·2
20	+ +	—	7·6	6·5
20	+ +	—	8·0	4·5
20	+	—	7·0	6·0
20	—	—	6·0	5·5
21	+	+ + +	6·7	7·4
21	+	—	7·2	6·3
21	+	—	6·6	5·4
21	+	—	6·0	6·0
21	+	+	6·0	6·5
22	+	—	6·7	4·5
22	+	—	6·8	6·5
22	+	+	6·8	5·5
23	+ +	—	6·8	5·9
23	+ + +	+ +	7·0	7·0
24	+ +	—	7·4	6·2
24	+	—	5·8	5·5
25	+ +	—	6·8	6·0
27	+ +	+	6·8	5·8
30	+ +	—	6·7	5·2

* + + +, indicate, great distension; + +, moderate distension; +, slight distension; —, no distension.

TABLE III

COMPARING THE SIZE OF THE PULMONARY ARTERY IN 50 SUBJECTS WITH TRIPLE RHYTHM (TYPE Ia) AND IN 50 SUBJECTS WITH DUAL RHYTHM

Measure of pulmonary artery enlargement		Cases with triple rhythm	Control cases with dual rhythm
Estimate at cardioscopy	Great	3	1
	Moderate	22	1
	Slight	22	6
	No enlargement	3	42
Pulmonary artery index	Average	6·7	5·7
	Less than 5·0	0	3
	5·0 to 5·9	2	26
	6·0 to 6·4	8	14
	6·5 to 6·9	18	5
	7·0 or over	22	2

Type Ib.—The Third Heart Sound in Right Ventricular Failure

Potain (1900) considered that protodiastolic gallop was not a state where the third heart sound was accentuated, but that it was actually a presystolic gallop in the presence of tachycardia. Although admitting the similarity between the physiological third heart sound and the protodiastolic sound, Gubergritz (1925) believed that there was a difference in the quality and intensity of the sounds. Wolferth and Margolies (1933) observed no essential difference in quality, location, time relation, or influence of posture and various manœuvres on the sounds. They considered that apart from the fact that the physiological third heart sound became increasingly rare with advancing age, the only criterion available for differentiation was the state of the cardiac function; when this was abnormal the sound could be arbitrarily classed as a gallop sound, but if no abnormality was detected the sound could be regarded as a physiological third sound. Lian (1934) believed that the protodiastolic gallop was produced by an accentuation of the physiological phenomenon connected with the third heart sound. I found that this form of triple rhythm can be distinguished from the physiological type by regarding its position of maximum audibility, the effect upon it of posture, its age incidence, and the state of the heart. Thus, it was best heard in the mitral area or beyond according to the degree of cardiac enlargement (Fig. 4); although better heard in the reclining posture it was usually audible in the upright posture; it was found even in elderly patients; it was associated with disease which produces enlargement and failure of the right side of the heart, namely mitral stenosis, hypertension, thyroid toxæmia, congenital heart disease, emphysema, pulmonary embolism, and pulmonary hypertension. Not all cases with these clinical conditions have triple rhythm, and the circumstances deciding its presence will be mentioned as each condition is discussed.

As in triple rhythm of Type Ia, so in Type Ib, the limb lead electrocardiogram was not in any way distinctive, except that it sometimes showed auricular fibrillation or right axis deviation.

The Third Heart Sound in Mitral Stenosis

In no other section of triple rhythm is opinion more confused than in the one dealing with the supernumerary heart sound in mitral stenosis. Lewis (1915 and 1934) stated that a wide duplication of the second sound initiating a sort of gallop rhythm occurred especially in cases of mitral stenosis with a slow heart rate. The extra sound in the early part of a long diastole was unrelated to auricular systole because it persisted when the auricles fibrillated; it was probably due to an unusual intensification of the normal third heart sound and tended to be confined to the region of the apical impulse. Conner (1927) described 10 patients, 4 with severe mitral stenosis, in whom he found an unusual variety of gallop rhythm; the supernumerary sound in early diastole was so exaggerated as to dominate the auscultatory findings resulting in a sound much louder than the two heart sounds which preceded it. White (1931) said that the protodiastolic gallop produced by accentuation of the third sound of the heart was relatively rare in mitral stenosis since it was masked by the diastolic murmur. Wolferth and Margolies (1933) differentiated between the opening snap of mitral stenosis and the physiological third heart sound or protodiastolic gallop, in that the snap was short and sharp, closer to the second sound, heard only in mitral stenosis, and in the third and fourth interspace over the body of the heart and not at the apex. Bramwell (1935) and Braun-Menendez (1938) regarded the gallop rhythm in mitral stenosis as the result of an exaggerated third heart sound.

Triple rhythm was specially sought in 70 patients with mitral stenosis, 25 of whom also had auricular fibrillation, and it was found in 44 (63 per cent). The added sound was heard in 21 of the 25 cases with fibrillation, and in 23 of the 45 with sinus rhythm. Thus triple rhythm was a much commoner finding with fibrillation present. Usually it was heard best towards the anterior axillary line over the displaced apex beat, but sometimes equally well in

the mitral area. The triple rhythm of mitral stenosis was always heard in the erect as well as in the reclining position. Although moderate tachycardia was found to accentuate most forms of triple rhythm, it had a deterrent effect on that of mitral stenosis with auricular fibrillation. In 14 of the 44 cases with triple rhythm the third sound was short and clear like the second sound, although generally less loud. The distance between the second and third sounds was compared with the same measurement obtained in cases of triple rhythm in health, i.e. Type Ia; in the healthy group the distance varied between 0·16 and 0·23 with an average of 0·19 sec. while in the presence of heart disease (Type Ib) it varied from 0·13 to 0·20 with an average of 0·18 sec., so the position of the third sound was the same in both the healthy and pathological groups (Fig. 9 and 10). In the remaining 30 cases the third sound was

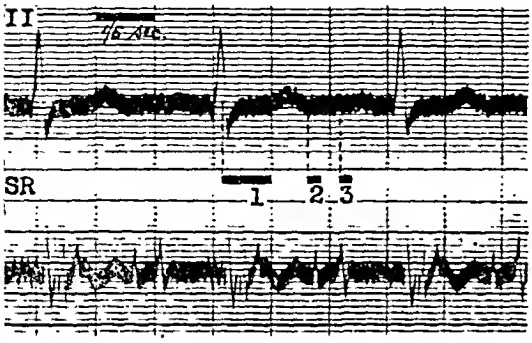

FIG. 9.—Triple rhythm, Type Ib, in a woman aged 28 with mitral stenosis. Diastolic murmur preceded first sound, and mid-diastolic murmur started at site of third heart sound.

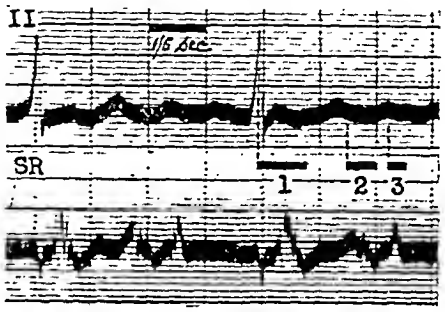

FIG. 10.—Triple rhythm, Type Ib, in a woman aged 46 with mitral stenosis and auricular fibrillation. Third heart sound was clear and not associated with murmur.

associated with the characteristic rumbling diastolic murmur of varying duration. This study of the relationship between the third sound and the mid-diastolic murmur in mitral stenosis has shown that they always coincide. I never found the diastolic murmur of mitral stenosis situated in the cardiac cycle in front of the third heart sound. It follows then that a diastolic murmur in mitral stenosis may occupy the late- or mid-diastolic period, but never the early part, so that an early diastolic murmur in the mitral area immediately following the second sound is evidence of aortic incompetence. Although the audibility of the supernumerary sound in mitral stenosis was sometimes disturbed in the mitral area by the diastolic murmur of aortic incompetence, it was never wholly obscured by it especially if auscultation was carried out towards the axilla.

An estimate of the size of the heart was made at cardioscopy in all cases of mitral stenosis that were specially examined for triple rhythm. The size of individual cavities was assessed and the presence and extent of pulmonary congestion. The pulmonary artery index was also recorded, and the results are given in Table IV. These appear to establish that in patients with mitral stenosis the finding of a triple rhythm gives some indication of the degree of cardiac enlargement. The size of the heart as a rule was least in those patients without (Fig. 11), and greatest in those with, triple rhythm (Fig. 12). When the heart was very large

TABLE IV

PULMONARY ARTERY INDEX IN 70 PATIENTS WITH MITRAL STENOSIS

Pulmonary artery index	44 patients with triple rhythm (Type Ib)	26 patients with dual rhythm
Average	8·4	6·3
Less than 7·0	5 patients	16 patients
7·0 to 7·5	10 ,,	8 ,,
7·6 to 8·9	14 ,,	2 ,,
9·0 or over	15 ,,	0 ,,

the supernumerary sound was commonly associated with the characteristic rumbling diastolic murmur. In view of this association between triple rhythm and the size of the heart it follows that this auscultatory sign does not always aid in the recognition of *early* mitral stenosis, but

FIG. 11.—Dual rhythm in a woman, aged 24, with mitral stenosis. Teleradiogram shows slight cardiac enlargement and P.A. index of 7·6.

it can tell something of the size of the right heart and it may often provide a valuable clue in differential diagnosis. Thus, in a case with auricular fibrillation where auscultation in the mitral area finds only a systolic murmur and no certain evidence of mitral disease, the presence of this type of triple rhythm will help to establish the diagnosis of mitral stenosis. This

FIG. 12. Triple rhythm, Type Ib, in a man, aged 52, with mitral stenosis. Teleradiogram shows considerable cardiac enlargement and high P.A. index of 9·4.

FIG. 13.—Triple rhythm, Type Ib, in a woman, aged 18, with thyroid toxæmia. Teleradiogram shows cardiac enlargement and high P.A. index value of 8·0.

triple rhythm is also expected in the fibrillation of thyroid toxæmia, and is not uncommon in prolonged hypertensive failure with fibrillation, but I have never met it in *senile* or *lone* fibrillation, where the heart was of normal size or thereabouts.

The Third Heart Sound in Hypertension

When heart failure makes its appearance in hypertension, triple rhythm is commonplace, but it is usually due to the presence of the fourth heart sound and not the third. Such patients are subject to paroxysmal nocturnal breathlessness and show pulmonary congestion on radiological examination. The familiar signs of right heart failure, namely, cyanosis, distension of veins in the neck, enlargement of the liver, ascites, and œdema of the ankles, are missing. When, however, left ventricular failure has been present for some time these signs often appear, and triple rhythm due to the third heart sound may then be elicited especially if tachycardia has not shortened diastole to such an extent as to cause fusion of the third and fourth sounds. This latter event has been described in a valuable paper by Wolferth and Margolies (1933) as summation gallop. Although the term is a useful one, it has limited clinical value by itself, depending as it does on findings in the phonocardiogram, and it is necessary to decide which supernumerary sound preponderates in the sound record after tachycardia has subsided. Many patients presenting triple rhythm, Type IIb, show this fusion of the two sounds; but when the effects of failure have been reduced by rest and the use of mercurial diuretics, and tachycardia has subsided with lengthening of the diastolic period

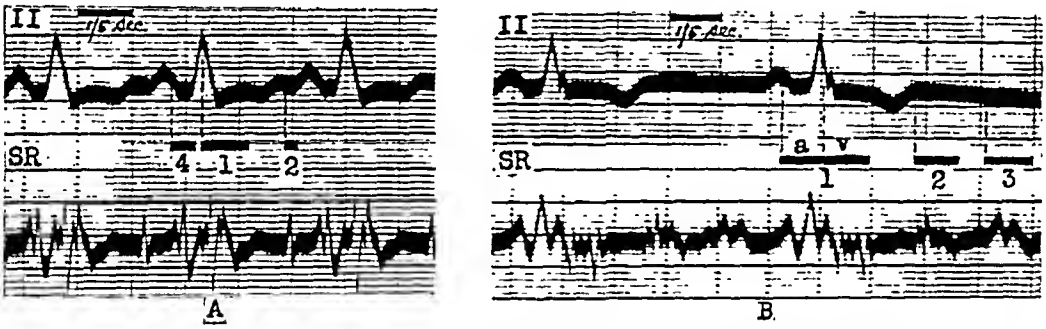

FIG. 14.—Triple rhythm, Type IIb (shown in A), changed to Type Ib (shown in B), after treatment with rest and mercurial diuretics. Male, aged 40, with hypertensive heart failure.

causing separation of the third and fourth heart sounds, the triple rhythm often changes from Type IIb to Type Ib (Fig. 14).

So far, I have found triple rhythm due to the third heart sound in 16 patients, but this does not mean that it is uncommon. Indeed, if we continue to search for this auscultatory sign in patients with hypertensive heart failure during the later phase of their illness, we shall often find it. The sound was heard best over the displaced apex beat near the anterior axilla, and although more distinct in the reclining posture it was also audible in the upright position. On cardioscopy these patients showed enlargement of the right auricle and ventricle, as well as the distension of the left ventricle and hilar congestion that constitute the earlier changes in hypertensive heart failure (Fig. 15).

Indicating, as I believe it does in hypertension, failure of the right heart as well as the left, this form of triple rhythm (Fig. 16) is a valuable sign. Of the fourth heart sound in hypertension it has been said that it is the cry of the heart for help (Obrastzow, 1905): if this metaphor is acceptable then we should recognize in the third heart sound in hypertension a more desperate appeal for assistance.

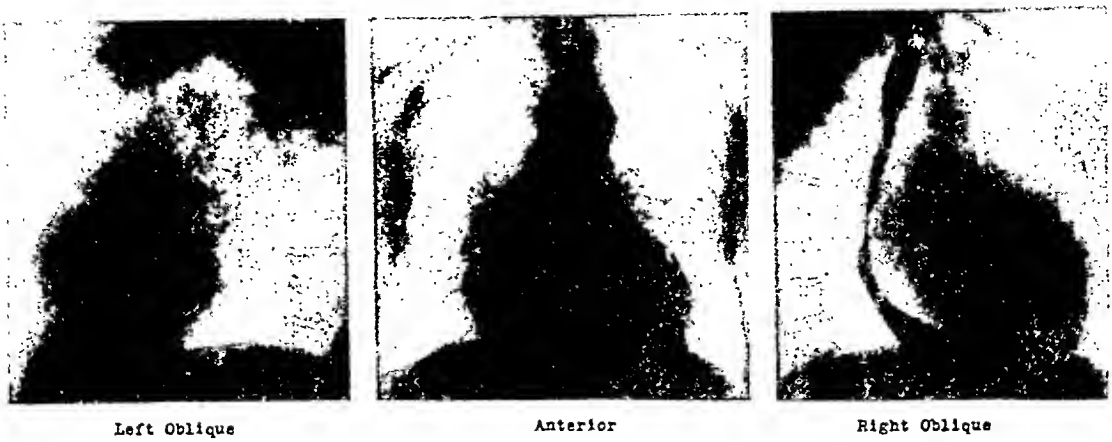

FIG. 15.—Triple rhythm, Type Ib, in a man aged 60, with hypertensive heart failure. Teleradiogram in anterior and oblique views show enlargement of right heart in addition to left ventricle, providing evidence of biventricular failure.

The Third Heart Sound in Thyroid Toxæmia

Triple rhythm due to the presence of the third heart sound was audible in the mitral area in the reclining and erect posture in 8 patients with toxic goitre. In all, tachycardia was moderate and was not regarded as a contributory factor. Hypertension was present in 2 of them. On cardioscopy some degree of cardiac enlargement and prominence of the pulmonary artery was present in 7: in 1 case there was enlargement of the left ventricle. As a rule then, when this form of triple rhythm was found in thyroid toxæmia, the heart on cardioscopy showed changes described by Parkinson and Cookson (1931). The special form characteristic of the goitre heart is based upon a combination of prominence of the pulmonary arc, the right heart, and the left ventricle. These changes are shown in a radiogram from a patient in this series exhibiting this type of triple rhythm (Fig. 13). No cardiac enlargement was found in a control series of cases with thyroid toxæmia who showed dual rhythm.

The Third Heart Sound in Congenital Heart Disease

I have never met with this form of triple rhythm in patients with congenital heart disease in the absence of right-sided cardiac enlargement. On the other hand, it has been absent in some cases showing considerable enlargement. The relationship between the actual congenital lèsion, the size of the separate cavities of the heart, and the presence or absence of triple rhythm is being studied. In the meantime it may be said that triple rhythm, Type Ib, is only found in subjects with congenital heart disease that has caused enlargement of the right side of the heart.

The Third Heart Sound in Emphysema

Clinical signs of cardiovascular changes are reported to be uncommon in emphysema. Parkinson and Hoyle (1937) said that simple clinical evidence that the heart was involved by the lung affection was usually wanting. Heart failure, although carefully sought with the aid of radioscopy in their series, was not common, and when it occurred it was a late event and almost invariably terminal.

I have looked for triple rhythm in patients with long standing emphysema and only discovered it in 5 (Fig. 17): in each case breathlessness from emphysema had been present for many years, but more recently heart failure with normal rhythm had set in, and with hepatic distension, ascites, and œdema in 3 of them. On auscultation in the mitral area triple rhythm,

Type Ib, was found, and the supernumerary sound was heard in the erect as well as in the reclining posture. Cardioscopy in these 5 patients showed cardiac enlargement and pulmonary congestion; the enlargement involved the right heart and pulmonary artery, and there was slight distension of the left ventricle although none had hypertension. The pulmonary artery index was 7·2, 8·0, 8·0, 8·2, and 9·5 in these five patients compared with an average of 6·2 in a control series of ten patients who had much emphysema without heart failure and presented a dual heart rhythm. In 80 patients with emphysema examined radiologically by

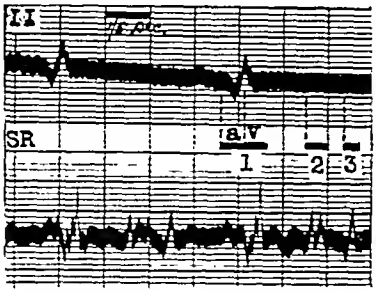

FIG. 16.—Triple rhythm, Type Ib, in a man, aged 71, with hypertensive heart failure.

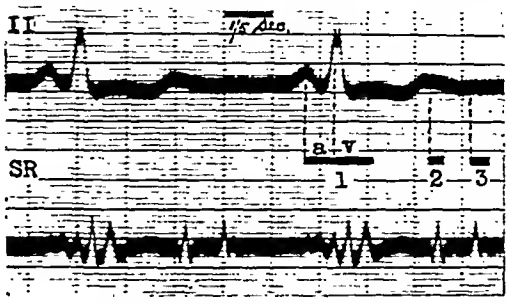

FIG. 17.—Triple rhythm, Type Ib, in a man, aged 58, with heart failure from emphysema.

Parkinson and Hoyle (1937), slight or moderate enlargement of the right auricle was present in 11, of the conus of the right ventricle in 33, and of the pulmonary artery in 22; a similar degree of enlargement of the right ventricle showed in 14 cases, but great enlargement was only met with in 4 patients, 3 of whom had heart failure.

Clinical and radiological examination of patients with emphysema permits me to say that triple rhythm, Type Ib, in these cases signifies prominent enlargement of the right heart and heart failure, and that it connotes the changes shown in Fig. 18. These changes were absent in patients with emphysema in whom a dual heart rhythm was heard (Fig. 19). This auscul-

FIG. 18.—Triple rhythm, Type Ib, in a man, aged 53, with heart failure from emphysema. Teleradiogram shows considerable cardiac enlargement and pulmonary congestion; pulmonary artery is distended with a P.A. index of 9·5.

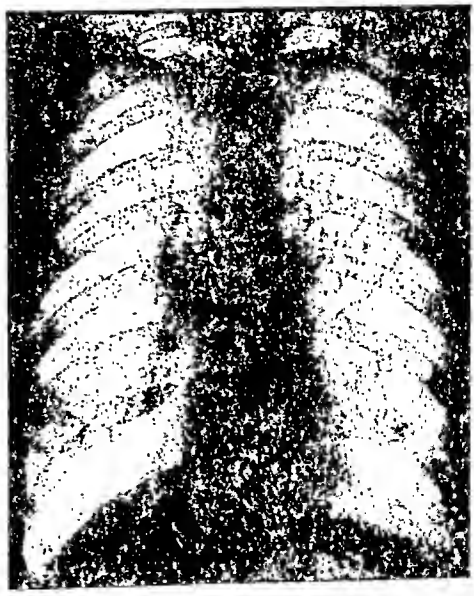

FIG 19.—Dual rhythm in a woman, aged 42, with emphysema and bronchitis and without heart failure. Teleradiogram shows no cardiac enlargement and a P.A. index is 6·3.

tatory finding of triple rhythm in emphysema is, therefore, a sign of prognostic significance for it signifies that any patient presenting it is unlikely to survive many months. Four patients reported here died within five months of finding this form of triple rhythm, and the other is precariously ill. The same triple rhythm has since been found in patients with pulmonary embolism and pulmonary hypertension.

A triple rhythm was found in 5 patients with constricting pericarditis but it was absent in 13 others. As the cases showing triple rhythm were young subjects, a further study of this group is being made to try to discover any factor which might determine the presence of the third heart sound.

Type II.—Addition of the Fourth Heart Sound

Triple rhythm caused by an added sound in late diastole is not less important in diagnosis and prognosis than triple rhythm resulting from an extra sound in early diastole. Since the adventitious sound in this form occupies a place that is later than the point at which the third sound occurs it may be called the fourth sound, and it immediately precedes the first heart sound. Actually it occurs during auricular systole so that it only precedes the ventricular moiety of the first heart sound (Fig. 1). As in the case of triple rhythm of Type I, so also in this variety designated Type II, there are two classes; in the first the supernumerary sound is produced by auricular systole and appears only when auriculo-ventricular conduction is delayed; in the second, although the sound is produced in or by the left ventricle affected by failure, regulated contraction of the auricle is again necessary for its production, and it is never heard in auricular fibrillation. Among 60 patients with triple rhythm due to the presence of the fourth heart sound, 14 belonged to the first group and 46 to the second. These two varieties will now be described.

Type IIa.—The Fourth Heart Sound in Delayed A-V Conduction

A sound produced by auricular systole is easily recorded, but the circumstances deciding its audibility are not altogether understood. In sound tracings from 16 healthy schoolboys, Bridgman (1914) recorded a presystolic sound in 11 of them. Since it was represented by a wave that usually showed displacement in only one direction, he concluded that it was subject to marked damping at the source. The wave occurred 0·02 sec. after the beginning of the auricular wave of the apex cardiogram, 0·07 sec. before the beginning of the first sound, and lasted 0·04 sec. Bridgman suggested that the sound was produced by tension of the ventricular walls caused by the onset of auricular contraction, and that there was a possible relationship between this sound and presystolic gallop. Lewis (1915) explained that the auricular sounds were not heard in the normal heart because the auricular and ventricular systoles occurred too close together. He also said that when contraction of the auricle was audible in certain cases of heart block, the human ear could sometimes detect a double sound and that sound records illustrated its dual nature. Reid (1921) also observed two components in the auricular sound itself where the second promptly followed the first and the vibrations of the second filled the interval of 0·05 sec. before the onset of the sound due to ventricular systole. After introducing a sound recording device into the œsophagus in 50 normal subjects, Taquini and Braun-Menendez (1935) were able to see the auricular sound clearly in every tracing. In 100 healthy students Braun-Menendez and Orias (1934) recorded the auricular sound on the surface of the chest in 20, while Caeiro and Orias (1937) using a more sensitive device recorded auricular vibration in 17 out of 20 healthy young adults. Braun-Menendez (1938) said that although it was difficult to recognize the auricular sound by auscultation this did not mean that it was inaudible; the impression gained by auscultation was that of an impurity of the first sound, or when the auricular sound was louder, a splitting of the first sound.

In the interpretation of sound records taken simultaneously with the electrocardiogram it is an accepted fact that the first sound is never recorded earlier than the R wave. Any sound wave visible immediately in front of the R wave must be the direct or indirect result of auricular contraction. In 32 sound records from cases in which a clear first sound was elicited on clinical auscultation, an auricular sound was recorded graphically in 30. In 20 of these the sound commenced at the end of the P wave in the electrocardiogram and just after in 4, but in 6 it started earlier and coincided with the descending limb of P. In some instances of isolated auricular contraction as in complete heart block the auricular sound also commenced early and once coincided with the summit of the P wave when it showed two separate groups of vibrations which were appreciated by clinical auscultation, giving to the auricular sound a dual character (Fig. 20 and 21). Since the supernumerary sound in delayed auriculo-ventricular

FIG. 20.—Auricular sounds recorded in complete heart block. Auricular wave immediately following the first heart sound (a) is suppressed.

conduction shows the same time relationship to the P wave as the auricular sound in records from subjects with dual rhythm, the sound is clearly caused by auricular contraction; it was never heard or recorded in auricular fibrillation. As in patients with complete heart block so also in subjects showing delayed A-V conduction the auricular sound is not always audible. In children and young adults the auricular sound was heard whenever the P–R interval in the electrocardiogram was prolonged, but not so in older subjects in whom it was often inaudible.

In the 14 subjects in this series where triple rhythm resulted from delayed A-V conduction (Fig. 22), the P–R interval measured from 0·20 to 0·33 with an average of 0·25 sec. Six of them were considered healthy after an examination that included cardioscopy, and the remaining 8 showed disease, this including mitral stenosis, coronary atheroma, and bundle branch block. Although a prolonged P–R interval was found in 7 patients presenting

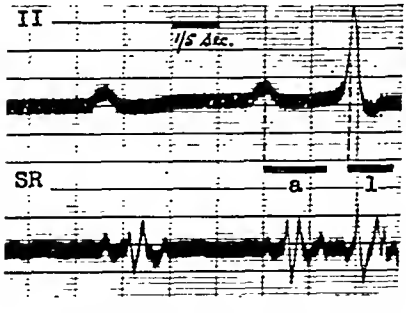

FIG. 21.—Isolated auricular sound in complete heart block showing early and late components; commencement coincides with summit of P wave. Tracings from a man, aged 60, with Stokes-Adams attacks. Auricular sound occasionally audible.

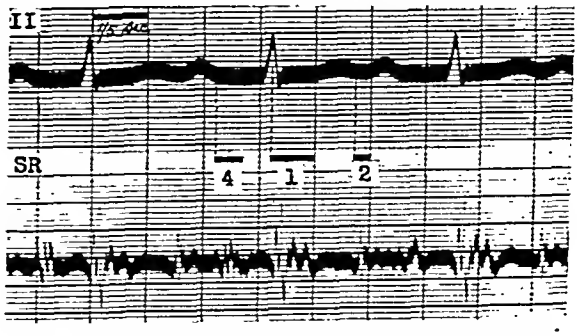

FIG. 22.—Triple rhythm. Type IIa, in a woman, aged 25, who showed no evidence of heart disease apart from delayed auriculo-ventricular conduction.

a fourth heart sound in left ventricular failure, it was not here regarded as having by itself initiated the supernumerary sound. Besides, the area over which the sound was heard was characteristic of the form of triple rhythm found in failure (Type IIb). Triple rhythm (Type IIa) was best heard a little internal to the mitral area and for a little distance around (Fig. 4). Although best heard with the subject reclining, it persisted in the erect posture. The rhythm was often made more obvious by induced tachycardia.

Sometimes four sounds could be heard in each cardiac cycle and the circumstances favouring this *quadruple rhythm* were found in the association of a delayed A-V conduction with a

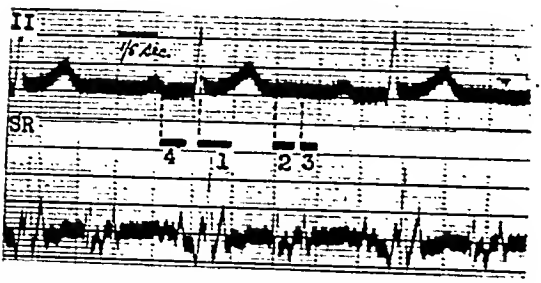

FIG. 23.—Quadruple rhythm caused by presence of fourth heart sound in delayed auriculo-ventricular conduction, and third heart sound in mitral stenosis, from a girl, aged 19.

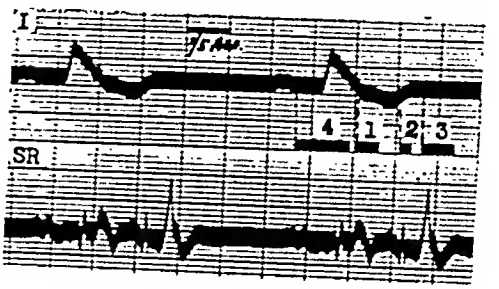

FIG. 24.—Quadruple rhythm caused by presence of fourth heart sound in delayed A-V conduction, and third heart sound in hypertensive failure, from a man, aged 44.

physiological third heart sound, or with a third heart sound in mitral stenosis (Fig. 23) or in prolonged hypertension (Fig. 24).

TYPE IIb.—THE FOURTH HEART SOUND IN LEFT VENTRICULAR FAILURE

For more than half a century this form of triple rhythm has been a physical sign familiar to many clinicians. There has been almost general agreement on its significance in diagnosis and in prognosis, and fair agreement on the mechanism of its production. Whenever opinion has been confused about its recognition it has usually meant that other varieties of triple rhythm have been included erroneously in this group rather than that a patient with this sound has been wrongly allocated to another group. Indeed, when a triple rhythm is alluded to as " gallop " without specific reference to its kind, it is understood as a rule to imply the type that is now to be described.

Among 60 patients with triple rhythm due to the presence of the fourth heart sound, left ventricular failure was the cause in 46, and the characteristics of this form have been determined from a clinical and graphic study of them. Hypertension had caused left ventricular failure in 41, and aortic incompetence, in 5. There were no cases of aortic stenosis.

The Fourth Heart Sound in Hypertension

As to the mechanism of this type of triple rhythm it is clear that two conditions are necessary for its production—left ventricular failure and a normally contracting auricle. Raised diastolic tension within the ventricle and increased intra-auricular pressure were mentioned by Mond and Oppenheimer (1929) as the cause of the supernumerary sound. Duchosal (1932) wrote that it was generally admitted that hypotonicity of the failing myocardium caused the ventricle to dilate suddenly and audibly under the influence of the auricular blood wave, so that auricular contraction on the one hand and ventricular hypotonicity on the other, were the two principal factors in the production of gallop rhythm. From his study of phonocardiograms Duchosal maintained that hypotonicity of the ventricle, which regulated the production and quality of the sound, could not by itself explain all the phenomena connected with gallop rhythm, and that it was necessary to consider the variation in the force and volume of the

auricular wave judged by changes in the interval between the P wave of the electrocardiogram and the supernumerary sound (the P–G interval). Since the sound appeared to come from the shock of the auricular blood wave on a hypotonic ventricle, he described it as auricular gallop, but Wolferth and Margolies (1933) considered the term misleading because there was no proof that the sound originated in the auricle.

Clinical features. The average age was 55 and only 3 were under the age of 40; this agrees with Bramwell's (1935) finding of 8 under 40 among 62 patients. Dyspnœa was always the outstanding symptom and in 30 this included cardiac asthma. Œdema of the ankles was found in 5 patients only and crepitations in the lungs or pleural effusion were present in less than half. In 38 the diastolic blood pressure was above 100, and the systolic was above 200 except in 6. In 3 patients a low blood pressure reading was ascribed to cardiac infarction. The cardiogram was usually abnormal and characteristic of hypertensive heart disease in that it showed left axis deviation, inversion of the T wave in lead I, and sometimes bundle branch block. Enlargement of the left ventricle, and sometimes of the other chambers in varying degree, was seen on cardioscopy. Pulmonary congestion, best seen at the hila, was also present in varying degree.

The supernumerary sound. The sound had a duller quality than the first heart sound which succeeded it. The interval separating the two sounds was brief, yet it was sometimes better appreciated by clinical auscultation than in the phonocardiogram where the sounds were often almost conjoined. It was usually heard along a line running from the displaced apex beat near the anterior axilla to the left border of the ziphisternum and was most intense at these two stations (Fig. 4). Thus among 41 patients it was heard at both places in 28, but better at the ziphisternum in 17 and at the apex in 11: in 8 it was heard at the apex only and in 5 at the xiphisternum only. I found no constant changes in the cardiac outline to correspond with the site of maximum intensity of the sound. These findings differ from those of Wolferth and Margolies (1933) who stated that in most cases the gallop sound was heard best in the neighbourhood of the apex impulse and only occasionally over or just to the left of the lower end of the sternum. They also said that such right-sided gallop occurred with dilatation of the right side of the heart and tricuspid insufficiency. The characteristic dual impulse associated with this type of triple rhythm was felt in most cases and was invariably present whenever the supernumerary sound was heard well. This was best appreciated by placing the naked ear to the chest when the impulse could be felt and the sound heard at the same time. As with other forms of triple rhythm this sound was better heard with the patient in the reclining position although it persisted in the erect. French writers have written on the association of tachycardia with this type of triple rhythm, and Bramwell (1935) has emphasized it as a constant finding. Naturally, tachycardia is common in patients with hypertensive heart failure, but I found this rhythm in five patients with a normal heart rate, and failed to produce it in seven with hypertension and heart failure by inducing tachycardia by exercise or ingestion of trinitrin (1/50 grain). None the less, whenever the triple rhythm is heard faintly, tachycardia usually accentuates it, and this accentuation is sometimes due to the superimposing of the third on the fourth heart sound, the summation gallop of Wolferth and Margolies (1933), as a result of shortening of the diastolic period (Fig. 25). Lewis in 1915 spoke of the effects of auricular fibrillation on this type of gallop rhythm. He said that if the rhythm was the result of a sudden rush of blood into the ventricle at the time of auricular systole one would not expect to meet with it in cases of fibrillation, and he had never found it.

The sound record. That the interval between the fourth and first heart sounds in this form of triple rhythm may often be better appreciated on clinical auscultation than in a sound record, has already been mentioned. The clear presentation of this triple rhythm appears to depend more on the intensity of the fourth heart sound and less on the length of the interval between the fourth and first sounds, although this plays a part whenever it is obviously pro-

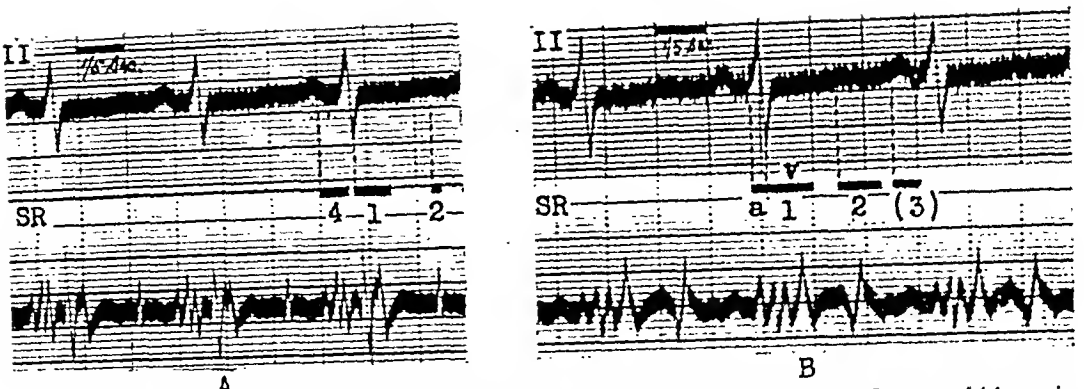

FIG. 25.—Triple rhythm, Type IIb (shown in A), changed to dual rhythm with splitting of first sound (shown in B), in a man, aged 69, with hypertensive heart failure, after treatment with rest and mercurial diuretics. The slower heart rate has caused separation of the third and fourth heart sounds. Third sound recorded but not audible.

longed. The intensity of the fourth sound probably depends on the degree of left ventricular failure; it is certainly increased by the frequent coincidence of the third sound which reinforces it. Duchosal (1932) has stressed the importance of the duration of the interval between the P wave in the electrocardiogram and the gallop sound in the sound record (the P–G interval). In connection with it he formulated two laws. The first law was that the P–G interval was an index of the seriousness of the affection; if the P–G was less than 0·05 sec. the prognosis was bad, but if greater the outlook was better. The second law was that the P–G interval varied in proportion to the improvement or aggravation of the case during the course of the illness. In cases presenting this triple rhythm, I have not found the start of the auricular sound in the phonocardiogram any nearer to the P wave of the electrocardiogram than in healthy subjects; it usually started at the end of the P wave as in the normal. Often when the start of the auricular sound wave appeared to coincide with the descending limb of the P wave or even with its summit—and such examples were common—it was found that the first part of the sound wave was the third heart sound which was continued into the fourth. When tachycardia subsided the third sound separated from the auricular sound which began at the end of the P wave. Although this summation effect of the third and fourth heart sounds is common in patients with left ventricular failure and tachycardia, I believe that the audibility of this type of triple rhythm depends a little on the summation effect but much more on the accentuation of the supernumerary sound itself from the ventricular failure.

The Fourth Heart sound in Aortic Incompetence

There were 5 examples of this, and left ventricular failure with normal heart rhythm was common to all of them. Hypertension was present in four and in one this was the result of coarctation of the aorta. Hypertension was absent in one case where the aortic leak developed quickly from bacterial endocarditis. With the progress of cardiac enlargement and failure in this patient, dual rhythm gave way to triple rhythm (Fig. 26). The clinical and graphic character of this supernumerary sound did not differ from that in hypertensive heart failure. It is likely that the fourth heart sound occurs as well in aortic stenosis and heart failure, but I have not yet met with a case.

Two conditions in particular have to be described in connection with triple rhythm, Type II: they are splitting of the first heart sound due to an accentuated but not displaced auricular sound, and splitting of the first sound in bundle branch block.

Splitting of the First Heart Sound

A splitting of the first sound results from a separation of its two natural sound components, the auricular and the ventricular. Although the designation of duplication may well convey

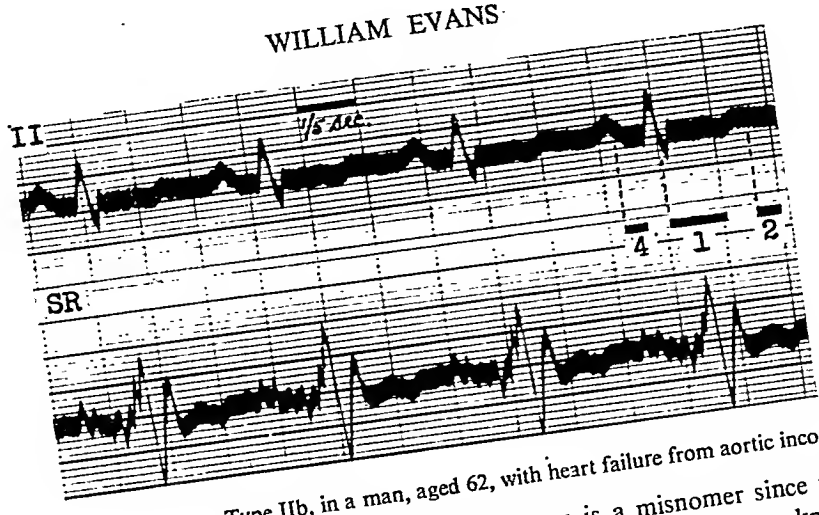

FIG. 26.—Triple rhythm, Type IIb, in a man, aged 62, with heart failure from aortic incompetence.

the impression gained by clinical auscultation, the term is a misnomer since the combined sound is never in fact repeated as a whole, but it often divides. It has been known for years that a " double first sound ", i.e. splitting of the first sound, was found in healthy subjects as well as in patients with heart disease. By itself this auscultatory finding has no special significance, except in bundle branch block which is to be considered separately, for it is only an exaggeration of the separation (and often in health) of these two constituent groups of vibrations. Cossio and Braun-Menendez (1935) found that in many cases where a diagnosis of splitting of the first sound had been made on clinical auscultation, the real cause of the auscultatory impression was the presence of an auricular sound. The frequency with which the auricular sound can be recorded phonocardiographically has already been mentioned, and it was found commonly in cases which showed neither splitting of the first sound nor the presence of a fourth heart sound. Usually only the second part of the auricular sound was evident and this was fused with the ventricular component of the first heart sound. A delay in auriculo-ventricular conduction (prolonged P–R interval), or bundle branch block, can each determine a splitting of the first sound, but a third variety of splitting is often heard in health and in the presence of a normal electrocardiogram, and the recognition of this is of great importance in clinical diagnosis. For this reason it is to be the subject of further cardiographic investigation.

Triple Rhythm in Bundle Branch Block

Lewis (1912 *b*) recorded the heart sounds in 4 patients with bundle branch block in whom a " duplication " of the first heart sound was heard on clinical auscultation. He said that the two sound elements could be dissimilar, in which case the first element was of smaller amplitude than the second and different from it in character. The first part commenced before, though the greater part of it coincided with, the ventricular complex. The second stood in much the same position as the normal first sound, but as a rule a little later, coming either 0·05 to 0·07 sec. after the opening of the electric deflections of the ventricle. The first element was properly speaking presystolic and occurred in part at least coincidentally with the auricular contraction; from its time relations it was clearly independent of ventricular systole. Lewis concluded that the double sound was not due to asynchronous action of the two ventricles resulting from the abnormal path taken by the contraction wave and leading to asynchronous closure of the valves. The P–R interval was prolonged in each of the two records that he published. From a clinical investigation of 41 cases of bundle branch block, Hill (1931) concluded that a duplicated mitral first sound was of little diagnostic value, because it occurred in cases other than bundle branch block and disappeared even while the block persisted. Campbell and Suzman (1932) reported an interesting case in which triple rhythm and bundle branch block disappeared simultaneously. Graybiel and Sprague (1933) described their

findings in 395 cases of bundle branch block; they said that diagnosis could only be made with certainty by the electrocardiograph. J. K. Lewis (1934) took sound records in 20 patients with bundle branch block; presystolic gallop was present in 9 and in 3 of these a presystolic impulse was felt; in 5 a duplicated first sound was heard. He came to the conclusion that the presence of triple rhythm in bundle branch block could be accounted for by the fact that both conditions occurred in the same general type of heart disease and under the same circumstances, and it was not related to the bundle branch block itself nor to asynchronism of the ventricles.

A triple rhythm was sought in 30 patients in whom a bundle branch block was shown in the electrocardiogram and it was found in 13. In 6 of these the triple rhythm was caused by the appearance of the fourth heart sound in delayed auriculo-ventricular conduction (Type IIa), and in the other 7 by the fourth heart sound in left ventricular failure (Type IIb). In only 2 of the remaining 17 cases with dual rhythm was the first sound clear in the mitral area; in 15 there was either a roughish systolic murmur with slurring of the sound sometimes simulating a presystolic murmur, or a splitting of the first sound. The relationship between a delayed auriculo-ventricular conduction time as shown by a prolonged P–R interval, and the incidence of triple rhythm in bundle branch block, was specially examined. A delay was present in 14 but not in the remaining 16. Out of the 14 cases with a P–R interval longer than 0·22 sec., 11 showed triple rhythm and 3 had dual rhythm. Among the 16 cases in which the P–R interval was less than 0·2 sec. there were 14 with dual rhythm. The remaining 2 showed triple rhythm (Type IIb) from left ventricular failure. These findings are summarized in Table V.

TABLE V

AUSCULTATORY FINDINGS IN 30 PATIENTS WITH BUNDLE BRANCH BLOCK

Incidence of triple rhythm		
Dual rhythm in 17	2—Clear first sound	
	15—Rough systolic murmur; slurred first sound; splitting of first sound	
Triple rhythm in 13	6—Type IIa	
	7—Type IIb	
Triple rhythm in relation to A-V period		
Prolonged P–R in 14 ..	3—Dual rhythm	
	11—Triple rhythm	6—Type IIa 5—Type IIb
Normal P–R in 16	14—Dual rhythm	
	2—Triple rhythm (Type IIb)	

The ventricular part of the first sound in the phonocardiogram of bundle branch block appears in relation to an S wave that is delayed because of a lengthening of the R–S interval. When this is considered alongside the fact that the P–R interval is also full and often prolonged in this condition, it is not difficult to understand why splitting of the first sound is common in patients presenting bundle branch block (Fig. 27).

Thus in the series reported here a pure first heart sound was uncommon (only 2 out of 30).

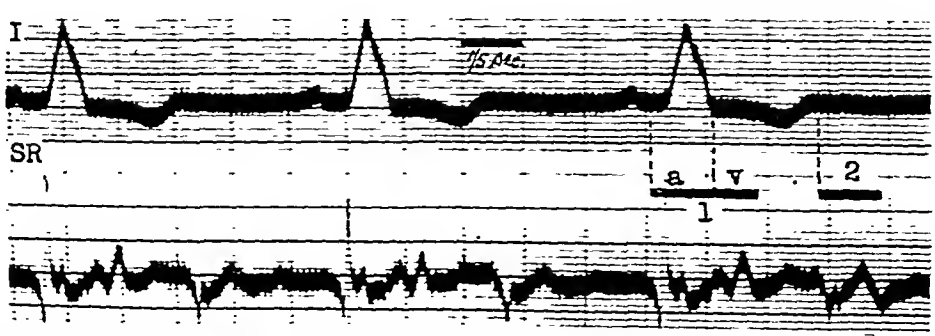

FIG. 27.—Splitting of first heart sound in bundle branch block in a man, aged 62. Auricular part of first heart sound is accentuated and ventricular part commences opposite delayed S wave of electrocardiogram.

In half the cases the sound was either obscured by a murmur or showed splitting. Triple rhythm in bundle branch block was never present unless there was delay in A-V conduction or left ventricular failure, and often both conditions existed together. It is because of this separation of the auricular and ventricular components of the first heart sound in bundle branch block that the condition may be referred to as one of " potential triple rhythm." The ease with which this rhythm becomes established either by a further slight increase in the P-R interval or at the first sign of left ventricular failure, is dependent on the already lengthened P–S interval which characterises bundle branch block.

Type III.—An Extra Heart Sound in Late Systole

Under the title systolic gallop, Johnston (1938) reported 21 patients in whom the systolic position of the supernumerary sound was shown in phonocardiograms. He pointed out that it usually happened in healthy hearts and that its importance lay in the fact that it was sometimes mistaken for a diastolic gallop. Laubry (1930) defined gallop rhythm as the result of the interposition of a third independent sound between the two heart sounds; it might occur during the short silence (systolic gallop) which was rare, or during the long silence (diastolic gallop) which was common and the only form which needed study. Among my 270 cases of triple rhythm there were 5 in which the supernumerary sound was situated in the systolic period. In all five a correct clinical interpretation was made before undertaking the phonocardiographic test which confirmed it (Fig. 28). Although casual auscultation may regard

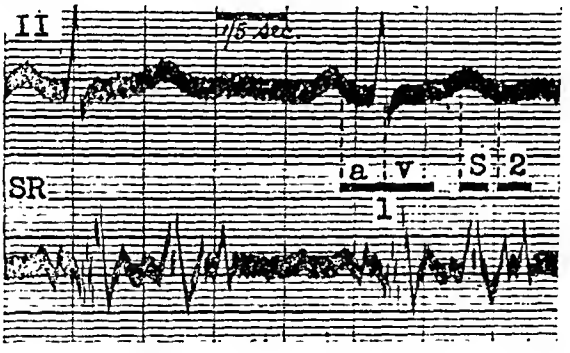

Fig. 28.—Triple rhythm, Type III, in a healthy man, aged 37. Added sounds are recorded in late systole and precede the second sound.

this as triple rhythm (Type I) a more careful examination will localize the supernumerary sound in front of and not after the second heart sound. It is possible to recognize the second of the three heart sounds as the supernumerary sound by paying attention to its character as well as its timing. Thus it can be made out that it is dull or muffled or like a click, compared with the clear second heart sound which immediately follows it. These characteristics were more readily appreciated when the stethoscope was moved away a little distance from the point of maximum intensity in the mitral area. In none of the five patients was there heart disease; in one the left ventricle was slightly enlarged from moderate hypertension. It is of interest that all five subjects had been informed after previous clinical examinations that they had " heart trouble," which shows that the importance of this innocent rhythm lies in its recognition.

Summary and Conclusions

Triple rhythm is the cadence produced by the recurrence in successive cardiac cycles of three separate sounds. The chief purpose of this work has been to classify triple rhythm in accord with findings on clinical, radiological, cardiographic, and sometimes pathological examination of the heart, in patients presenting this auscultatory sign. Splitting of the first

sound at the apex or of the second sound at the base of the heart are not included in its scope. The investigation has shown the need for discarding the terminology hitherto in use for triple rhythm and adopting one that is based on the clinical condition and avoids any preoccupation with the mechanism of the extra sound. As soon as it becomes the custom to listen specifically for a sound in addition to the more familiar first and second heart sounds, triple rhythm will be found to be common, perhaps as common as dual rhythm in patients sent for examination of the heart.

When the position of the adventitious sound in the cardiac cycle was considered alongside the clinical state of the patient in 270 cases with triple rhythm, it was possible to place them in three groups. As a rule, even under the handicap of fairly severe tachycardia, the position of the extra sound could be told by auscultation, aided by the clinical data, and before phonocardiography was used for scientific support.

In the first group (Type I), consisting of 205 cases, the added sound was the third heart sound occurring in early cardiac diastole. This group comprised of 125 healthy subjects, and 80 patients with right ventricular heart failure. The innocent triple rhythm (Type Ia) is distinguished from that due to right heart failure (Type Ib) by regarding the site of maximum audibility of the sound, the effect of posture upon the sound, and the health or disease of the heart. In Type Ia the sound is best heard a little internal to the normal apex in the mitral area, it is usually audible only in recumbency, and it is found in young healthy persons. It is uncommon after 24 (20 out of 125 in this series) and after 40 it is seldom if ever heard. On cardioscopy some degree of prominence of the pulmonary artery is a characteristic finding—an association in keeping with the common incidence of this auscultatory sign in children where a prominence of the pulmonary arc is a recognized feature of the normal radiogram. In Type Ib the sound is loudest at the apex, which is displaced according to the degree of cardiac enlargement; it persists in the upright as well as in the recumbent posture, and it is associated with disease that causes right ventricular enlargement and failure, such as mitral stenosis, hypertension, thyroid toxæmia, congenital heart disease, emphysema, pulmonary embolism, and pulmonary hypertension. Triple rhythm was present in half the cases of mitral stenosis and in four-fifths of those with auricular fibrillation. More often than not the third heart sound in mitral stenosis was joined with the characteristic diastolic murmur. When the third heart sound was present in hypertensive failure there was clinical evidence of failure of the right as well as of the left ventricle (biventricular failure), and cardioscopy showed enlargement of the right heart in addition to that of the left, and pulmonary congestion characteristic of the early phase of this failure. Patients with thyroid toxæmia showing a third heart sound had general enlargement of the heart and a prominent pulmonary artery; indeed the finding of this triple rhythm in each case predicted such changes while a series in which there was dual rhythm were without cardiac enlargement. Not all cases of congenital heart disease showed the third heart sound; but, when they did, enlargement of the right side of the heart, although probably not the only criterion, seemed essential to its appearance. The few patients with heart failure from emphysema, in whom considerable enlargement of the heart was seen at cardioscopy, showed this triple rhythm. A series of cases of emphysema with dual rhythm showed slight or no cardiac enlargement and no failure, so that the finding of the third heart sound in emphysema implies the presence of cardiac enlargement and failure and predicts a serious prognosis.

In the second group (Type II) the fourth heart sound is added during auricular systole and at the end of ventricular diastole. There were 60 patients with this variety of triple rhythm. In 14 of them it was the outcome of delayed A-V conduction (Type IIa). Not all cases whose P–R interval exceeds 0·2 sec. will show triple rhythm, although in young subjects, few will fail to present it. In 46 patients the extra sound appeared during left ventricular failure (Type IIb), where auricular action, although probably not the direct cause of the sound, is essential for its production, because it disappears with the onset of auricular fibrillation. Hypertension

is the usual cause of the left ventricular failure initiating this variety of triple rhythm, but occasionally it is the result of aortic incompetence. The added sound in these cases, although audible as a rule over the displaced apex beat, is usually best heard near the xiphisternum, and since it is accompanied by a palpable impulse, the rhythm is well appreciated by direct auscultation whereby the impulse is felt and the triple rhythm is heard simultaneously. This rhythm is often annulled when failure symptoms abate after the use of mercurial diuretics, but later it may give way to triple rhythm (Type Ib) when failure of the right heart has become added.

Bundle branch block with its wide P–R and QRS periods is a potential source of triple rhythm on this account for the fourth heart sound will appear when the P–R interval lengthens further or when the left ventricle begins to fail.

In the third, and least important group (Type III), an extra sound is added in late systole. It occurs in health, and almost its only importance lies in distinguishing it from the third heart sound. Since tachycardia is usually absent, its recognition on clinical auscultation is not difficult.

Triple rhythm is a common auscultatory sign, and it can be of great aid in the diagnosis of cardiovascular disorder. It should be sought specifically in every case, and when found, the position of the supernumerary sound in the cardiac cycle should be traced, and its significance determined in the light of clinical findings and in accordance with some classification such as that here proposed.

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TREATMENT OF SUBACUTE INFECTIVE ENDOCARDITIS WITH HEPARIN AND CHEMOTHERAPY

BY

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The incidence of bacterial endocarditis in rheumatic heart disease has been reported by various workers to be between 4 and 17 per cent, while in congenital heart disease it is between 14 and 22 per cent. The condition has been regarded by most physicians as uniformly fatal, though undoubtedly some mild and a few severe cases occasionally recover as Libman (1934) and Hamman (1937) have pointed out. By examining only reported series of cases of infective endocarditis treated by non-specific means, Lichtman and Bierman (1941) found that 6 out of 634 had undergone spontaneous cure. There are also reports of small epidemics of apparently proven cases in which the recovery rate has been high (Oille, Graham, and Detweiter, 1915, 1924, and Salus, 1920). Since the introduction of the sulphonamide drugs, there have been many reported cures and consequently a great revival of interest in the diagnosis and treatment of this condition. Having observed the successful cases reported by Kelson and White (1939) treated with sulphapyridine and heparin, we undertook this investigation, primarily to study the combined method of therapy with heparin and sulphonamides.

The lesion is a focus of relatively avirulent organisms enclosed in a mass of platelets and fibrin on a damaged valve. In 90–95 per cent of cases, the organisms are of the *Streptococcus viridans* type. The method by which they form these foci is debated: they may be embolic in the damaged valve or deposited on the surface with the platelet thrombi. Von Glahn and Pappenheimer (1935) have suggested that the lesions are grafted on to an active rheumatic endocarditis in most cases. The blood of these patients contains a very high antibody titre against the infecting organism and this factor alone tends to localize any transient bacteræmia. The platelet thrombi thus provide an ideal nidus for bacterial proliferation, providing as they do an excellent barrier from the bacteriocidal action of the blood, and situated upon a tissue that has the most sluggish reaction in the body, because there is minimal blood vessel and leucocyte invasion in the damaged valves. The infection is able to continue in the valve only if the deposition of fibrin exceeds the rate of invasion of leucocytes and it is upon this balance that the ultimate fate of the patient depends. Treatment will therefore depend upon either preventing the further deposition of fibrin or killing the organism by methods such as chemotherapy.

HEPARIN AND CHEMOTHERAPY

Friedman, Hamburger, and Katz (1939) tried the first concept by using continuous intravenous heparin to bring about a prolongation of the clotting time during a period of two weeks or more and so slowing the deposition of fibrin. Since their original report some 5 cases at least have been treated and all have died. Kelson and White (1939) combined both concepts of treatment and reported 4 cases cured out of a total of 7 treated. This combined therapy has now been given to more than 70 reported cases of which 7 have survived. Such treatment, however, is not without danger. The risks of continuous intravenous therapy in

seriously ill patients for a period of fourteen days are considerable. The increased fluidity of the blood carries with it still more dangers. Cerebral hæmorrhage and cerebral emboli have been attributed to the prolonged clotting time, and Kleiber (1940) and Witts (1940) have reported renal hæmorrhage. All these complications can occur without any therapy, and it may be difficult to prove statistically that there is any increased risk in the use of heparin. In our Case 5, we considered that the patient's death was directly due to heparin. Prior to therapy his condition had been good, his clotting time had been markedly prolonged by heparin, and his temperature adequately controlled by sulphapyridine; and at autopsy the vegetation was small and suggested that healing was taking place: however, he died suddenly of cerebral hæmorrhage whilst under treatment. In most reported cases, fairly adequate prolongation of the clotting time was obtained. In four of our cases it seemed inadequate in spite of using the doses of heparin recommended. Some of the preparations used appeared to be lacking in potency (cf. Petch, 1940). It is difficult to believe, in the absence of experimental proof, that healing of the lesion could take place in the short space of two weeks. It is also fair comment that no case has yet been reported cured by the use of combined therapy in which complete control of the infection had not already been attained by chemotherapy alone, so that the role of heparin becomes extremely difficult to evaluate. At present, opinion is against the further use of heparin as now administered because the dangers appear to outweigh the uncertain advantages.

Case 1. A man, aged 22, was admitted complaining of cough, palpitation, and sweating of five weeks duration. On examination, he had mitral and aortic valvular disease, an enlarged spleen, petechiæ, and red cells in the urine. The blood culture was positive for *S. viridans*. His temperature varied between 101° and 102° F. He had a moderate degree of anæmia. Chemotherapy (sulphapyridine 45 g. during the first 13 days followed by 62 g. and prontosil 60 g. over the next 24 days) caused an immediate reduction of his temperature. On the seventh day, intravenous heparin in saline was given (750,000 units in 10 pints normal saline over seven days). No definite effect upon the clotting time was noted. He died five weeks after this and two weeks after stopping chemotherapy, in congestive failure. There was no autopsy.

No adequate deductions can be made from this case. He probably died from rheumatic carditis with the infective process temporarily controlled by the chemotherapy. There does not appear to be any evidence that the heparin played any role in the maintaining of normal temperatures or indeed that it exerted any action at all in the dosage given. The extra fluid may have played some part in the subsequent congestive failure. A normal temperature is not infrequently seen in the terminal stages of this disease.

Case 2. A man, aged 30, was admitted on 13/10/39 complaining of pyrexial attacks and general malaise following dental extraction five months previously. Examination showed a good general condition, clubbed fingers, and signs in the heart of a patent ductus arteriosus. Blood cultures grew *S. viridans*. The temperature varied between 97 and 101° F. After two short trials of chemotherapy with immediate control of the pyrexia, sulphapyridine was given for one month. Blood cultures became negative immediately and on the ninth day, intravenous heparin in saline (1·6 g. in 23 pints of saline in 10 days) was given. Only slight prolongation of the clotting time, from 5 to 15 minutes, was obtained. The temperature remained normal for eight weeks apart from one episode of chest pain suggestive of a pulmonary embolus. Following a severe hæmolytic streptococcal throat, he again began to run a high temperature. Prolonged chemotherapy (101 g. over five weeks) again brought about a remission. During this period the remainder of his septic teeth were extracted and a number of blood cultures were negative. The patient felt well and had put on weight whilst his blood count had risen to over four million. He left hospital in May, 1940.

Nothing further was seen of him in spite of repeated requests until he was again readmitted. He had worked for six months on a light job, but two months prior to admission, had had a recurrence of all his previous symptoms. Examination showed the typical café-au-lait colour, splenomegaly, and Osler's nodes, while the heart showed in addition to the original lesion, signs suggesting involvement of the aortic and the mitral valves. Blood cultures were again positive for *S. viridans* and the pyrexia varied between 99–101° F. Chemotherapy was again started and 150 g. sulphapyridine were administered over 45 days. The temperature was fairly well controlled on this regime, only occasional temperatures of 99–100° being observed: the white cells were not depressed in spite of a moderate degree of anæmia (2·6 million). At first it seemed that a further remission would be induced, but after four weeks his condition began to deteriorate and chemotherapy was subsequently

stopped. He was discharged home and died three days later, about two years after the onset of his illness. There was no autopsy.

Here, the onset appeared to be precipitated by his dental extractions and the source of the infection may have been there. Sulphapyridine was probably the main factor in producing the good remission that he had early in his illness. Heparin had very little part and very little effect in prolonging the clotting time. In addition to his congenital heart lesion, he presented symptoms and signs suggestive of active rheumatism, involving the heart and especially the aortic valves. If such was the case, he was probably more liable to a flare up of the infective process. We considered that this patient's life was prolonged by the treatment.

Case 3. A girl, aged 19, was admitted 27/3/40, complaining of shortness of breath and swelling of her joints. Examination showed petechiæ, a mitral systolic murmur and thrill, and an early diastolic murmur at the aortic area. Her temperature varied between 101 and 103° F. Blood cultures were positive for *S. viridans*. Sulphapyridine brought about an immediate reduction in her temperature and after 40 g. had been given, it was discontinued, with an immediate reversion of her temperature to the previous levels. One week later, chemotherapy was again instituted and again the temperature was controlled. After 50 g. had been given over 9 days, the white cells fell to 400. She reacted well to blood transfusions and the fortuitous occurrence of an abscess of the buttock. Following her recovery, her condition remained unchanged for the next five weeks. A further 32 g. was given without any ill effects upon the white cells but after five days, the pyrexia reappeared. A further course of 16 g. had no effect at all upon the temperature. On 12/7/40, chemotherapy was again started in adequate doses with control of the temperature, and on the seventh day intravenous heparin in normal saline was given (2·25 g. in 15 pints of normal saline over 150 hours). On the third day, however, splenic infarction occurred, and the following day she developed signs at the left base with recurrence of temperature and general deterioration; heparin was accordingly stopped. Chemotherapy was continued for two further periods, 51 and 70 g. being given, with only slight control of the temperature. Her condition during this period deteriorated only slowly. Eventually five months after admission she went into coma and died, having during this time received 270 g. of sulphapyridine.

Autopsy showed numerous infarcts in lungs, kidneys, and brain. The heart weighed 560 g. with extensive vegetations on the mitral, aortic, and tricuspid valves.

Chemotherapy may have played a part in prolonging the life of this patient. Heparin had no effect except in the possible production of emboli. Again one failed to effect adequate prolongation of the clotting time with the doses of heparin that were given. Following agranulocytosis, further chemotherapy was not given without trepidation, but there was no reduction of the white cells in spite of the full doses of sulphapyridine, 182 g. in all. At first the organism seemed to be susceptible to the drug but eventually became resistant. The experience in this case made us persevere with more continuous chemotherapy.

Case 4. A man, aged 41. Eight months previously he had begun to run intermittent temperatures following a sore throat, gradually losing weight and developing malaise. He had had numerous small hæmoptyses. For the past five months he had been continuously in bed. Examination showed a very ill man with signs of aortic and mitral disease, splenomegaly, clubbed fingers, and a high swinging temperature. Blood cultures were positive for *S. viridans*. Whilst in hospital, he had a number of attacks of paroxysmal auricular fibrillation. His temperature responded immediately to chemotherapy and on the sixth day intravenous heparin and saline was started (1·5 g. in 4 pints of normal saline over six days). No prolongation of clotting time beyond 21 minutes was obtained, his normal being four minutes. On this therapy he deteriorated rapidly and began to run a temperature. He was allowed home, still taking sulphapyridine, and died a few days later. There was no autopsy.

This patient was already seriously ill when therapy was started and his course did not appear to be influenced in any way.

Case 5. A man, aged 36, was admitted, complaining of pyrexial attacks and malaise following dental extraction four months previously. Examination showed a mitral systolic murmur and thrill, finger clubbing, petechiæ, and splenomegaly. Blood cultures were positive for *S. viridans*. His temperature varied between 99 and 101° F. In spite of these findings, his general condition was good. Sulphapyridine was started with an immediate reduction of temperature. Owing to nausea and vomiting, a concentration greater than 9·9 mg. per 100 c.c. was never attained, the average being about 5 mg. On the seventh day heparin in saline was given intravenously (8·25 g. in 16 pints over 13 days). Satisfactory prolongation of the clotting times was achieved, up to 60 minutes.

There was an immediate rise of temperature with the intravenous therapy which settled again in two days. His blood count fell from four million to two and a half, and his condition which had been good began to deteriorate rather rapidly. He died suddenly from cerebral hæmorrhage on the thirteenth day of intravenous therapy.

Autopsy showed extensive cerebral hæmorrhage with previous emboli and extensive retroperitoneal hæmorrhage. The heart showed a small vegetation on the mitral valve less than ¼ inch long. Microscopical section of the valve and vegetation showed much fibroblastic activity and giant cell formation.

We considered that the death of this patient was almost directly due to heparin therapy and that had chemotherapy alone been employed, he would have had an excellent chance of surviving. As a consequence of the experience of this and the other cases, we were reluctant to submit further patients to the combined therapy before we had made an extensive trial of chemotherapy alone.

Chemotherapy Only

The second aspect of therapy is that of exerting bacteriostatic or bacteriocidal influences upon the organisms themselves. Innumerable substances have been administered by mouth, subcutaneously, and intramuscularly, without any effect until the sulphonamide group of compounds was tried, though Osgood (1942) has recently claimed good results from a modified treatment with neoarsphenamine. Experimentally it is difficult to show how the sulphonamides have produced these cures. Friedman (1941) has shown that sulphapyridine has little penetrating power into the fibrin barrier round the focus of bacteria. He reported unsuccessful results in 12 cases and concluded as a result of his experimental and clinical findings that chemotherapy was of no avail. Duncan and Faulkner (1941) confirmed these experimental findings but they showed in addition, that the sulphonamide derivatives would be included in the clot if they were given prior to the formation of the clot. The number of reported cures supports this observation and should refute Friedman's statement and Katz (1941) belief that no case has ever been cured by chemotherapy. Since the bacteriocidal power of the blood is already adequate to deal with any organism liberated but not with the source of the organisms themselves, the suggestion put forward by Duncan and Faulkner that the drugs act by being incorporated in the clot seems to be the most logical and probable mechanism.

Lichtman and Bierman (1941) found that 12 out of 200 reported cases of subacute infective endocarditis had recovered. They also pointed out that of 45 cases treated with hyperpyrexia in addition, 9 recovered. Such figures, though not dramatic and probably from rather selected series with milder cases, do offer some improvement upon the era before chemotherapy. Indeed, Graybiel and White (1942) suggest that it is now probable that one case in twenty recovers.

During the past three years, we have observed 20 cases (including the 5 to whom heparin was also given) to whom the sulphonamide group of derivatives was given in adequate doses. Of these, 5 were totally unresponsive to either sulphathiazole, sulphapyridine, or sulphonamide; 12 cases were moderately controlled with temporary antipyretic effect, and 3 showed complete remission of the pyrexia. Case 1 received sulphonamide for 37 days apparently with complete control of the infection before dying of congestive failure. It is difficult, however, to draw any conclusions from this case. Case 6 was completely relieved of his symptoms but died a year after the onset of his infection, with congestive heart failure. Case 7 has now been apyrexial for seven months and has had a normal sedimentation rate for five months.

Case 6. A man, aged 21, was admitted complaining of general malaise and high temperature for 13 weeks. He had had chorea when 4 and probably acute rheumatism when 18. He had been otherwise well and active.

Examination showed a pale but fairly well-built man with early finger clubbing. There was a systolic murmur at the apex and a marked musical diastolic murmur at the base. The tip of the spleen was just palpable. There was no petechiæ. Three blood cultures were negative. An X-ray examination of the heart did not show any enlargement.

For the first ten days in hospital he ran an irregular temperature to 102° F. With the administration of sulphapyridine (6 g. daily), the temperature fell to normal on the third day. For the next 8 months, only on three occasions did the temperature reach 99° F. Four days after starting therapy, he developed pain in the left hypochondrium and the spleen became more easily palpable. This disappeared after two days and was not felt again. After one month, the dose of sulphapyridine was halved to 3 g. daily and this dosage was continued for seven months, a total of 730 g. being given without any nauseating or obviously deleterious effects.

The sedimentation rate fell from 38 mm. per hour (Westergren) on starting therapy to 6 mm. per hour after six weeks and remained below this until his final illness.

His blood count gradually rose to 4,700,000 red cells (from 4·1), to 94 per cent hæmoglobin (from 80), and to 7500 white cells. His white blood cells count fell to 4900 on one occasion, but usually remained between 5500 and 6000, the polymorphs averaging 60 per cent.

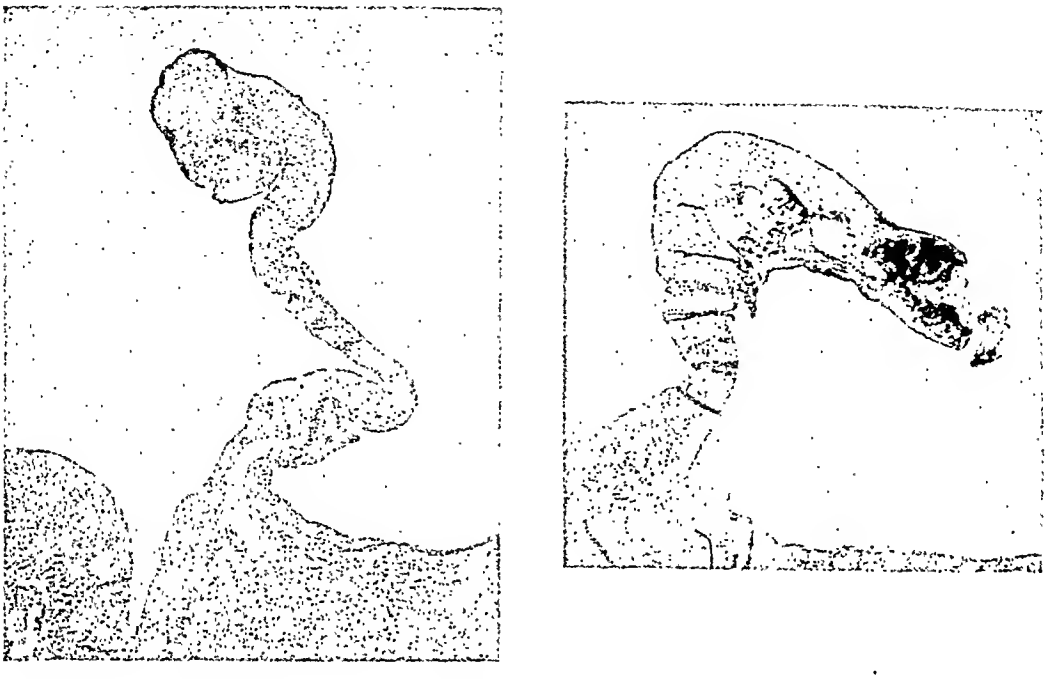
He was discharged from hospital for further convalescence 14 weeks after admission. The only

FIG. 1.—Interior of the left ventricle showing the aortic valves with two perforations, through which fibres have been passed. The endocardium round these perforations is well healed. The calcified vegetation is seen on the adjacent cusp. All three cusps show evidence of chronic rheumatic endocarditis.

disquieting feature was mild anginal pain on exertion, and a rapid pulse rate varying between 95 and 100. Over the next few months, he was seen regularly and it was noted that his heart was gradually enlarging. In spite of this, he felt well and was able to start work for a few hours daily as a laboratory technician. Unfortunately at the end of his first week he developed a severe cold and sore throat. Two weeks later he was readmitted with congestive failure, marked jaundice, and signs of consolidation at both bases. He died three days after admission.

Autopsy. Pleural cavities, a large amount of straw-coloured fluid. Lungs, both congested and œdematous with diffuse bilateral bronchopneumonia. Heart, enlarged and dilated, weighing 590 g. Left auricle, normal; left ventricle hypertrophied and dilated, with incompetence of the mitral valve and some thickening and shortening of the chordæ tendinæ. Aortic valve (Fig. 1) incompetent, the edges thickened. On edge of right cusp a pedunculated and calcified vegetation. Left cusp, two small perforations with healthy endocardium round them. Right ventricle, dilated and hypertrophied; right auricle, normal. Liver, congested. No evidence of perisplenitis or old infarcts in the spleen. Kidneys, a few typical healed scars of old infarcts.

Microscopical examination. Heart muscle showed considerable interstitial fibrosis. No Aschoff's bodies were seen. Sections through the calcified vegetation showed complete covering with endocardium (Fig. 2 and 3) with no evidence of any bacteria or inflammatory reaction. Sections through the two perforations of the valves also confirmed the diagnosis of healed infective endocarditis. Sections of the lungs showed diffuse bronchopneumonia with polymorphonuclear infiltration. The kidneys appeared to be normal except for the signs of congestion.



A B

FIG. 2.—(A) Section through the central cusp passing through the edge of the two perforations. Magnification ×11·7. (B) Section through the base of the calcified vegetation and the valve cusp, showing the extensive calcification. Magnification ×10·8.

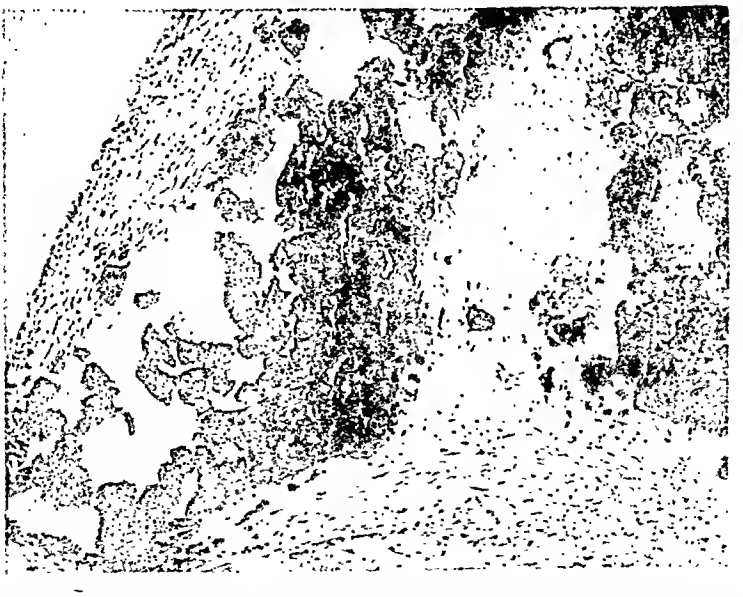


FIG. 3.—Section as in (B) showing the tip under high power. A number of foreign body giant cells can be seen round the edge of the calcification. There is a good endocardial covering and no evidence of any polymorphonuclear or lymphocytic infiltration in the extensive fibrous tissue. Magnification ×100.

This patient was able to take over 700 g. of sulphapyridine during seven months of therapy, showing no obvious deleterious effect and maintaining a good appetite the whole of the time. Examination of the sections of the heart valves showed that he had indeed been cured, but that the damage wrought upon the aortic valve had thrown too great a strain upon the myocardium and caused his death. This possibility is always present, so that even though the infection is cured, the residual lesion may be sufficient to kill the patient or cause him to be a permanent invalid. There are, however, an adequate number of reported cured cases who are earning their living, enough to indicate that the majority do attain a fair degree of recovery. There was no evidence of myocarditis in the sections such as has been reported by French and Weller (1942) following the use of the sulphonamide drugs.

Case 7. A milk-roundsman, aged 29, was admitted to hospital, complaining of pain in the left side and in the back of two weeks' duration. He had had rheumatic fever at the age of 18 for fifteen weeks, since followed by intermittent pains and swelling of his joints. Over the previous ten months he had noticed some shortness of breath and lassitude, insufficient, however, to keep him from his work. Ten weeks prior to admission, he had severe pain in his back for four days. Four weeks later, he had a severe cold and sore throat. Following this, he had severe soaking night sweats and began to feel really ill. Two weeks prior to admission, he again developed pain in the back and left loin which persisted until admission.

Examination showed a fairly well built man with a slight café-au-lait coloration, marked finger clubbing, and slight clubbing of the toes. There were no nodules or petechiæ. His teeth were grossly infected and carious. The heart was not enlarged. The mitral first sound was accentuated with a loud rough systolic murmur and thrill and soft mid-diastolic murmur. The sounds at the aortic area were normal. His blood pressure was 120/85. The spleen was just palpable. The urine contained a cloud of albumen, fatty and hyaline casts, and occasional red cells. His blood count was red cells 4,320,000 hæmoglobin 78 per cent and white cells 9150 with 75 per cent polymorphonuclears. The blood cultures showed 12 and 5 colonies per c.c. of *S. viridans*. His sedimentation rate was 81 mm. per hour (Westergren method). His temperature varied between 98° and 102° F. On commencing sulphapyridine (6 g. daily), his temperature fell to 99° F. As a normal temperature had not been produced in nine days, three injections of intravenous T.A.B. vaccine was given on alternate days. Following a moderately good reaction, his temperature became normal and has remained normal since except for three further T.A.B. injections given six weeks later. Slight nausea but no vomiting was produced by the sulphapyridine during the first five days, but thereafter he was able to take the drugs without any discomfort. After ten days, the dosage was reduced to 4 g. daily and on this dosage he maintained a blood stream concentration of sulphapyridine varying between 14 and 21 mg. per 100 c.c. His white cells never fell below 8500, his average count being 10,000 with 55 per cent polymorphs. His septic teeth were extracted in the sixth week of therapy and he was allowed to sit out of bed at the end of the ninth week. At this stage his pulse varied between 90 and 100 beats per minute while his sedimentation rate had dropped to 6 mm. per hour.

He was finally discharged at the end of his fourteenth week of therapy to a convalescent home, having put on two stone in weight whilst in hospital. Sulphapyridine was continued with two grams daily for a further four weeks. In all he took 400 g. of sulphapyridine without any ill effects. At present, he looks extremely fit, has some dyspnœa on moderate exertion, but is without any signs of bacterial endocarditis and his sedimentation rate is normal.

This patient appears to have attained a complete remission from his infection. He is still limited in his activities by his mitral stenosis. The consistently high blood levels of sulphapyridine may have played some part in his recovery. It was also of interest to note that his temperature only fell to normal after intravenous T.A.B. vaccine as advocated by Soloman (1941). We are not, however, inclined to attribute any definite role to this treatment as a factor in his recovery. At no time during chemotherapy did we experience any anxiety about the effect upon the white cells or kidneys.

Of the twelve cases that made some response to chemotherapy, all eventually became resistant and died. None of them took the drugs without showing much nausea, necessitating discontinuance of therapy in some cases even though there seemed to be some control of the infection. These toxic manifestations are the chief difficulty in the treatment and frequently prevent adequate concentration of the drug in the blood stream. One of these cases received sulphapyridine, sulphadiazine, and sulphathiazole in succession, 340 g. in all over nine weeks without a successful result although the temperature was fairly well controlled. There was,

however, much nausea and intolerance to the drugs and concentration above 6 mg. per 100 c.c. was not attained. In such cases, even if there is not complete control of the infection, it is felt that prolonged therapy is justified in view of the experience reported by Heyman (1940) in which some weeks elapsed before the patient became afebrile and eventually obtained a complete cure.

Agranulocytosis was encountered once (Case 2) but this responded well to therapy. Subsequent chemotherapy was controlled by white cell counts on alternate days, the leucocytes remaining consistently between 7000 and 10,000. Only a few cases of agranulocytosis have been reported, e.g. Leach *et al.* (1941) and Rinkoff and Spring (1941). Smith, Sauls, and Stone (1942) gave 894 g. of sulphanilamide in 73 days of continuous therapy to one of their patients who had been fit and well at the time of the report for 29 months. Thomas (1942) in considering the dangers of agranulocytosis in prolonged therapy in the prophylaxis of rheumatic fever, pointed out that in no instance had any toxic effects been seen after the first few weeks of treatment and that agranulocytosis had never been observed after the fiftieth day of chemotherapy given for any condition. We agree that the risks of chemotherapy are slight and in view of the seriousness of the disease being treated, that they may be neglected though routine weekly counts should be made.

In an effort to minimize the nauseating effect of the drugs, they have been administered in a mixture containing sulphapyridine or its equivalent 1 g., citric acid ½ g., nicotinic acid 25 mg., mucilage q.s., aq. menth. pip. ad. ½ oz. For the first few weeks of therapy, this was always given with food or milk. Ascorbic acid 300 mg. daily was also given in some cases including Cases 6 and 7, primarily to counteract the deficiency induced by any prolonged infection. Recently, however, Thompson (1942) has shown that ascorbic acid under experimental conditions markedly diminishes the toxic effects of sulphapyridine probably through its oxidizing properties. Vitamin A, 5000 units, and Vitamin D, 1000 units, were also administered daily to most patients.

The persistence of a slight temperature in some cases may well be due to the presence of active rheumatic fever. It is important therefore that prolonged rest in bed should be employed in any case where it seems likely that cure is probable, in order to allow the heart to recover as fully as possible from the serious infection to which it has been subjected. Even so, as we have pointed out above, the case may proceed to a fatal termination as in Kelson and White's Case 1 and our Case 6. Occasionally, as Jones and Bland (1939) have pointed out, the sulphonamide drugs may cause a fatal relapse in rheumatic myocarditis. The temperature may also be due partly to the drug itself. In one of our cases which eventually died and in Case 4 of Leach *et al.* this appeared to be so.

The evaluation of any therapy in infective endocarditis is made difficult by the uncertainties of diagnosis. In a patient with pyrexia, the presence of three out of four criteria, a valvular murmur, splenomegaly, positive blood cultures, or embolic phenomena, are usually accepted as sufficient evidence. The only absolute proof, however, is the presence of the lesion at autopsy. The diagnosis in Case 6 was confirmed at autopsy and Case 7 showed all four of the criteria usually accepted for the diagnosis. In early or mild cases, these criteria may not be fulfilled, and in such cases with recovery, cure cannot be claimed. These difficulties were well illustrated by one further case.

A woman, aged 26, was admitted with repeated hæmoptyses and slight pyrexia. Examination showed a pale sweating woman with signs of mitral stenosis. Whilst under observation she had repeated episodes of chest pain and hæmoptysis, and began to run a high swinging temperature. At the same time, she developed an aortic diastolic murmur and a collapsing pulse. Repeated blood cultures were negative. She showed no response to salicylates. Some control of the temperature was obtained with sulphthiazole, but after 45 g. had been given as her condition appeared to be deteriorating, she was taken home by her relatives. Now, 15 months later, she has a normal temperature but still an occasional hæmoptysis. The diagnosis of infective endocarditis therefore has been revised and it is considered that acute rheumatic carditis explained the whole illness.

Summary and Conclusions

Five cases were treated with combined chemotherapy and intravenous heparin. All died, and in one this was probably due to the heparin therapy.

Twenty cases (including the five treated with heparin) were studied under treatment with sulphonamide derivatives. Five were totally unresponsive, twelve were moderately controlled. Life was prolonged in some but all eventually died. Three cases became apyrexial; one died after 45 days of normal temperature, but as there was no autopsy, neither the diagnosis nor the state of the lesion could be determined. A second died one year after the onset of his infection and eight months after the control of his pyrexia by sulphapyridine: autopsy showed healed lesions of infective endocarditis. The third is well and working at his occupation as a milk-roundsman, at the present time, now twelve months after his discharge from hospital.

Intravenous heparin did not prove of value in our cases and, as others have found, should not be used in these cases.

Prolonged chemotherapy offers a chance of cure to a few patients though the great majority will not be so benefited. The dangers of such prolonged therapy are small and should not weigh against the chances of a successful outcome.

We wish to thank the Physicians of the Birmingham United Hospital for permission to study these cases. The cost of heparin was defrayed by a grant from the Medical Research Council.

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PROCEEDINGS OF THE CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND

The SEVENTH ANNUAL GENERAL MEETING of the Cardiac Society of Great Britain and Ireland was held at St. Thomas' Hospital, London, on Friday, June 11, 1943.

CHAIRMAN: SIR MAURICE CASSIDY

The Chairman took the chair at 10.15 a.m.
52 Members, 12 Temporary Members, and 2 Visitors were present.

PRIVATE BUSINESS.

1. The minutes of the last meeting having been printed in the Journal were confirmed and signed.

2. The accounts, audited by Donald Hall and Chamberlain, were presented by the Council and approved, the balance being £43 6*s.* 11*d.* The Council had decided that no subscriptions should be collected for the year 1943/4.

3. The following new Members were elected:—

Ordinary Members	*Associate Members*
Hugh Barber	W. Trevor Cooke
A. G. Biggam	Alastair Hunter
Athelstane Hill	E. V. Sharpey-Schafer
B. A. McSwiney	W. K. Stewart

Seven associate members were re-elected for another period of three years.

4. Leslie Cole, Cambridge, and John Parkinson, London, were elected members of the Council for the years 1943–47.

5. The Secretary was re-appointed for another year, and William Evans was again asked to act as Assistant Secretary.

6. The Secretary reported as follows.
   (*a*) He had learnt with pleasure from a letter from America that Charles Laubry, whose obituary notice had been published in the Journal, was still alive and in good health.
   (*b*) The Committee appointed to report on the scheme for the treatment of juvenile rheumatism had submitted their report, which would be dealt with by Bruce Perry later in the discussions; and the Council had instructed the Secretary to get in touch with the Pædiatric Association, who had drawn up a similar report, to see if it was possible for the two bodies to issue a joint report.
   (*c*) The Council had asked Cassidy, Chamberlain, and Campbell to reply to a letter from the Director General of the E.M.S. about the rehabilitation of cardiac patients, and the Council hoped after some explanations and additions to publish the substance of this communication.
   (*d*) The Council had instructed the Secretary to write to the Registrar of the Royal College of Physicians, to express their opinion that, if any subdivisions of physicians were made in the list of consultants, cardiologists should be included; and that if societies of specialists were consulted on this and allied questions the Cardiac Society should be included among such societies.

   [The Secretary has since received a letter from the Registrar of the Royal College of Physicians reporting that this letter had come before the Standing Joint Committee of the three Royal Colleges and that it had been decided to add the Cardiac Society to the list of Societies who are willing to give advice when asked to the Standing Joint Committee of the three Royal Colleges.]

(*e*) The Council had re-appointed the Editors of the *British Heart Journal* for a second period of five years; and had decided that no change should be made in the members of the Editorial Board for another year.

7. During the afternoon discussion, the Society, on the proposal of Geoffrey Bourne, instructed the Secretary to write to the Minister of Health, the Minister of Pensions, and the Minister of Labour and National Service, stating that the Cardiac Society was willing to help, if asked to do so, in a consultative capacity or by appointing members to serve on a committee, in relation to war or to post-war problems of a cardiac nature.

Short Communications.

Potassium and the Electrocardiogram

E. P. Sharpey-Schafer

(Published in full; pp. 80 and 85)

Observations on Diphtheritic Carditis

H. Cookson reported that preliminary observations on 54 cases of diphtheria suggested that death from circulatory failure was confined to the un-immunized child. Clinical, cardiographic, and pathological investigations were made on 7 children, aged 3 to 12 years, who died between the 3rd and 56th day of the illness. Death resulted from circulatory failure except in one in whom it occurred on the 56th day from the effects of neuritis. With early death (up to the 8th day) the course was progressively downwards from the onset, with widespread hæmorrhages. Clinical signs of congestive failure were absent, but triple rhythm was present and the cardiogram was abnormal. One patient showed terminal ventricular tachycardia. With death from the 9th day onwards the condition of the throat and neck cleared up, and then, after a varying interval of spurious convalescence, signs and symptoms of congestive and peripheral failure appeared. Liver congestion was invariably present. A progressive slowing of the heart rate was characteristic of this phase. Chief cardiac signs were a diffuse precordial impulse, disappearance or lateral extension of the apex beat, and triple ryhthm. Only once did a systolic murmur appear. The blood pressure fell progressively for some days before death. Cardiography showed axis deviation, depression of the S–T segment, and conduction disturbance. The S–T depression might be found within 48 hours of the onset; it had some diagnostic value for it had not been found in controls with other acute infections. In the 2 cases with the longest course the cardiogram showed low voltage and T changes, the type of curve found in the adult.

Post-mortem, there was increased heart weight and thickening of the wall especially of the left ventricle. There were intracardiac ante-mortem thrombi in 2 cases. Histologically the striking change was muscle degeneration to the stage of necrosis in some areas. Inflammatory and reparative processes were slight. Bilateral pleural effusions were present in 2 cases. The liver showed degeneration in the 2 cases with the shortest course, and venous congestion, usually intense, in the others. A normal heart muscle was found in the case that died on the 56th day, as a result of diaphragmatic and other palsies, after recovering from severe congestive failure. This last finding supports the general, but not universal, view that when recovery from diphtheria does occur, however severe the attack may have been, no permanent cardiac lesion remains.

An Unusual Case of Paroxysmal Tachycardia

C. G. Parsons

(Published in full; p. 187)

Complete and Partial Heart Block

Maurice Campbell

(To be published in full)

Incomplete Bundle Branch Block

C. W. C. Bain

(To be published in full)

Acute Left Auricular Failure

Crighton Bramwell and Morgan Jones described two cases of mitral stenosis, with unexpected death from acute pulmonary œdema in mid-pregnancy. In both cases a severe button-hole mitral stenosis was found at autopsy but only a presystolic murmur was present during life. The maintenance of ventricular filling in mitral stenosis was discussed and it was shown that, as chronic left auricular failure develops, ventricular filling is maintained by a gradual increase of left auricular diastolic pressure, which leads to chronic pulmonary congestion. It was suggested that when severe mitral stenosis is combined with a greatly hypertrophied left auricle, as in the two cases described, ventricular filling depends largely on auricular systole. In these circumstances, if the left auricle failed suddenly, a rapid rise of auricular diastolic pressure would occur and lead to acute pulmonary œdema.

Pseudo-angina and Para-œsophageal Hernia

S. W. Patterson described pseudo-anginal symptoms in association with para-œsophageal hernia. In cases of strangulation of the herniated viscera an acute upper abdominal crisis may simulate an attack of coronary thrombosis. Less severe symptoms of cramp-like pain in the lower chest behind the sternum, and radiating through to the back, up to the throat, and sometimes to the left shoulder, may simulate angina pectoris. These symptoms tend to follow conditions bringing about increased intra-abdominal pressure, especially posture, rather than effort and emotion. In some cases, thought to be neurosis, cardiac symptoms may arise from para-œsophageal hernia.

The mechanism of these symptoms may be (*a*) vascular, strangulation, obstruction, ulceration, hæmorrhage; (*b*) from pressure on lungs and heart; (*c*) from stimulation of the vagus terminations; or (*d*) from stimulation by stretching of the muscle-sensory fibres of the phrenic, which Mathison (Mathison, G. C. M., *Rev. Neurol. Psych.*, 1912, 10, 553) showed experimentally in dogs, cats, and rabbits caused a rise of blood pressure and increased depth of respiration.

The Electrocardiogram in Myotonia Atrophica

William Evans said he had examined the electrocardiogram in 9 cases and had found some characteristic change in all of them. The commonest was a prolongation of the P–R interval (with phases of 2:1 heart block in one case) slurring of the QRS complex, and electrical variation. Among the commonest clinical signs were a small pulse, a low blood pressure, and slurring or splitting of first heart sound, or triple rhythm depending on the degree of delayed A-V conduction. On cardioscopy the heart was small in 4 cases and enlarged in 3 where the P–R interval was much prolonged.

Trevor Cooke said that over the past six years he had made essentially similar observations in 9 cases. Thus the blood pressure tended to be low, being 100 systolic or lower in 5 cases and in none was it higher than 120. There was a tendency to bradycardia, the usual pulse rate being between 65 and 75 whilst two cases had pulse rates below 55. The heart (in 7 cases examined radiologically) was small in all. An electrocardiogram was recorded in 8, and only 2 (aged 17 and 22 years) had entirely normal tracings. One man, aged 39, with marked wasting and moderate myotonia showed almost flat tracings. Subsequent treatment showed a slight increase in voltage comparable with his general clinical improvement. At that stage, intramuscular prostigmin and adrenalin and intravenous quinine had no effect upon the cardiogram. Two further cases consistently showed curves suggesting recent coronary occlusions and the other three showed abnormal QRS complexes, low voltage, and low T waves.

Discussion on the Significance of Systolic Murmurs (*Morning Session*)

Noble Chamberlain deprecated the use of the word "functional" to indicate murmurs that were associated with non-valvular organic changes in the cardio-vascular system. He felt that the terms "significant" and "insignificant" might be helpful. *Significant* murmurs could include those systolic murmurs that arise from valvular heart disease or from regurgitation through an enlarged valve ring or from pathological dilatation of the vessel or chamber into which the blood is travelling. *Insignificant* murmurs would include those commonly described as physiological or cardio-pulmonary and those occurring as a temporary phenomenon in anæmias and fevers. In deciding whether or not a systolic murmur was significant, he felt that the pendulum had swung too far and that there was a tendency to regard all systolic murmurs as harmless.

In the case of basal systolic murmurs, he thought that the diagnosis of aortic stenosis might be possible in the presence of a harsh systolic murmur especially associated with radiological evidence

of left ventricular enlargement but without a thrill or the characteristic anacrotic pulse. Further, murmurs which become increasingly rough are more likely to be associated with organic changes.

In the case of the mitral systolic murmur, undoubtedly the most difficult, he suggested that roughness, wide conduction, and persistence and length were characteristics more often associated with organic defects than had lately been admitted. These murmurs are usually present both in the erect and recumbent postures though more in the latter, and they are not materially modified by respiration. Whilst murmurs having these characteristics did not necessarily indicate the presence of organic disease, they could not be regarded lightly, especially in children and in the presence of a rheumatic history. It was therefore very important to consider them in relationship to the radiological and electrocardiographic changes. It was common in children to find such significant murmurs becoming associated in a few years' time with other and clearer evidence of organic heart disease. On the other hand, it was freely admitted that in adults these significant characters might never be associated with other signs, though they were more likely to be found with diastolic murmurs or with cardiac enlargement than murmurs presenting insignificant qualities, namely, quietness and inconstancy or modification by posture and respiration.

Chamberlain referred to the common occurrence of a mid-sternal systolic murmur especially at such routine examination as is employed for recruits. He thought that if such a murmur was harsh, care should be taken to exclude the presence of a thrill, a radiologically globular heart, or right ventricular preponderance in the cardiogram, and that if any of these signs were present, the diagnosis of patent interventricular septum was justifiable. If the murmur occurred alone, even though rough, he felt it could be disregarded.

WILLIAM EVANS spoke of two varieties of mitral systolic murmurs, the one in late systole, and the murmur of mitral incompetence. The former was not uncommon; it was loud and long, and was usually best heard with the subject in the upright posture. It was not difficult to recognize because it was separated from the first heart sound by a distinct interval; indeed, the murmur was nearer to the second heart sound than to the first. The murmur assumed importance on account of the frequency with which it was regarded as evidence of mitral disease. When 40 such cases were examined clinically and by cardioscopy the heart was shown to be healthy, so that the innocent nature of the murmur had been established.

Unlike aortic incompetence, *mitral incompetence* presented no constant pattern on clinical, radiological, or pathological examinations; indeed, a systolic murmur appeared to be the only sign allotted to it, but this murmur was also frequently present in mitral stenosis, aortic incompetence, aortic stenosis, and hypertension. Two criteria might be set up to test the presence of mitral incompetence in these conditions, namely, disease and/or dilatation of the mitral valve, and enlargement of the left auricle. These were sought radiologically and at necropsy in cases where a mitral systolic murmur was associated with one of these four conditions. They were absent except in mitral stenosis. Even in mitral stenosis Evans thought that the lesser effect of mitral incompetence, admittedly present, did not merit specific mention in diagnosis, for the term mitral stenosis was a comprehensive one standing for mitral disease caused by rheumatism, showing systolic and diastolic murmurs and characteristic changes in the contour of the heart as seen radiologically, commonly giving rise to auricular fibrillation which at the start responded favourably to digitalis, and often complicated by intra-cardiac thrombosis and embolism. Further, since the presumptive diagnosis of mitral incompetence hindered precise diagnosis of heart disease, Evans asked for the disuse of the term.

THE PLACE OF CARDIOLOGY IN A CO-ORDINATED MEDICAL SERVICE (*Afternoon Session*)

F. R. FRASER spoke of the hospital services.

If it is assumed that the post-war hospital scheme will be based on the division of the country into areas, each capable of providing all the normal hospital and consultant services, there will be a "key" hospital in each area and the specialists and special units for the area will normally be situated at the "key" hospital. A number of such areas will come within the sphere of influence of a medical school and its teaching hospital; and within each area there will be subsidiary hospitals and perhaps health centres that look to the "key" hospital for support and inspiration. There should be in each area a physician specially trained and experienced in the diagnosis and treatment of cardiac and circulatory disorders. He should be on the staff of the "key" hospital, and be available for consultations at the subsidiary hospitals of the area. In association with the "key" hospital, there should also be a special hospital or unit in suitable surroundings for the treatment and rehabilitation of selected children and young adults with cardiac damage resulting from rheumatism.

BRUCE PERRY spoke of the care of the rheumatic child, some of his points being the same as those made in the preliminary reports on these subjects of the committees set up by the Cardiac Society and by the Pædiatric Association.

Acute rheumatism produces such serious effects in children that it is important all cases should be brought under skilled treatment as soon as possible. Compulsory notification seems the only method of ensuring this, and should include all cases of acute rheumatism, chorea, rheumatic heart disease, and heart murmurs of doubtful significance in children. The latter need to be included (though possibly they should be referable to the clinic rather than notifiable) to differentiate the murmurs due to rheumatic heart disease from those of less significance.

The need for hospital treatment for a long period calls for special hospitals equipped with school teachers and school apparatus. Such hospitals should be of the open-air type in the country, and could sometimes be combined with those for the treatment of children with tuberculosis. It is probably desirable that the children should, in the first place, be admitted to the main children's hospital or the children's department of the main general hospital, and should be transferred from there to the special hospital to complete their treatment. The suggested cardio-rheumatic clinic should be held in the main hospital of the region, and in addition to full medical facilities including those for radiography and electrocardiography would need an almoner's department and adequate secretarial assistance to see that the necessary help was given and that home conditions were as satisfactory as possible, and that arrangements could be made for getting children up at regular intervals as needed. It would seem disadvantageous to make a break between this clinic and the clinic continuing to help these patients when they have reached adult life and needed advice as regards occupation, pregnancy, etc., and therefore a closely related clinic for adults, perhaps in the evening, would be desirable.

MAURICE CAMPBELL spoke of the place of cardiology in relationship to general medicine, and of the cardiologist to the general physician.

The advantages of the physician specially trained in heart disease are so obvious, both from the technical knowledge of X-rays and electrocardiograms and from the clinical knowledge of heart problems, that anything to be said on the other side is sometimes forgotten. Even from the point of view of the patient himself, the suspected diagnosis of heart disease may be wrong, and the problem may be a general medical one, as there are so many general diseases overlapping with cardiac problems; it is, therefore, essential that the cardiologist should be a good general physician. Apart from the necessity for an interest in psychology, one need only mention anæmia, hyperthyroidism, diabetes, reneal disease, and certain diseases of the chest presenting themselves as dyspnœa or pain, to realize the need for wide general medical knowledge. Secondly, both from the point of view of teaching and general organization of a medical service, a man who is also a general physician is more useful. The ordinary-sized hospital is not large enough to justify the appointment of a cardiologist, and only when a medical centre is large enough to need ten or twelve physicians can one devote himself almost whole-time to cardiology.

It would probably be agreed that neurology and dermatology should be the first medical specialities to be separated off, but many would think that cardiology and diseases of the chest would be the next most important to separate. Sometimes in the smaller centres these two can be combined. The separation of pædiatrics as a medical speciality, except in so far as it applies to the care of children up to 12 or 18 months, would appear to be a mistake, as medicine makes no dividing line for age, and the disease—whether of the nervous system or of the heart or of the lungs—often starts in childhood and continues into adult life.

As regards the training of the cardiologist, no one should take up this work until he had done two to five years' general medical work of registrar status after ordinary house appointments and (if it is so decided in the future) passing the examinations and holding the appointments necessary for consultant status, and after this, two to five years' training in the special problems of cardiology.

He concluded (1) that all larger centres should have a cardiac department with a physician in charge and a second physician or registrar and the necessary technical help, and (2) that no one should be recognized as a cardiologist who has not already become a recognized general consulting physician.

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Luncheon was served at St. Thomas' Hospital, by the kindness of the Governors of the Hospital. As it was not possible to arrange a formal dinner, the members met at 1 Devonshire Place, W.1, by the invitation of the Chairman and John Parkinson.

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